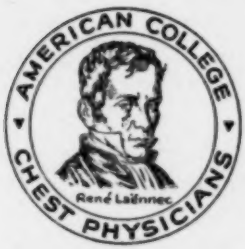
VOLUME XVIII NUMBER 3

# DISEASES

## *of the*

# CHEST

OFFICIAL PUBLICATION

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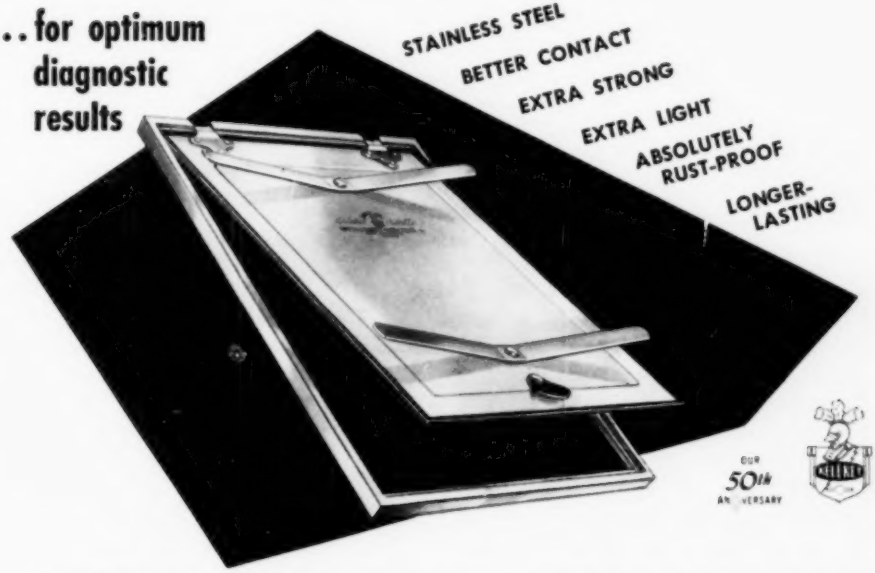


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# DISEASES *of the* CHEST

OFFICIAL PUBLICATION

OF THE

AMERICAN COLLEGE OF CHEST PHYSICIANS




EXECUTIVE OFFICE
500 North Dearborn Street, Chicago 10, Illinois
MURRAY KORNFELD, *Managing Editor*

VOL. XVIII SEPTEMBER 1950 No. 3

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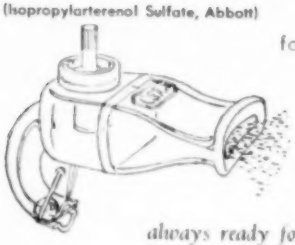

1. Krasno, L. R., Grossman, M. I., and Ivy, A. C. (1949), The Inhalation of 1-(3',5'-Dihydroxyphenyl)-2-Isopropylaminoethanol (Norisodrine Sulfate Dust), J. Allergy, 20:111, March. 2. Krasno, L. R., Grossman, M., and Ivy, A. C. (1948), The Inhalation of Norisodrine Sulfate Dust, Science, 108:476, October 29.

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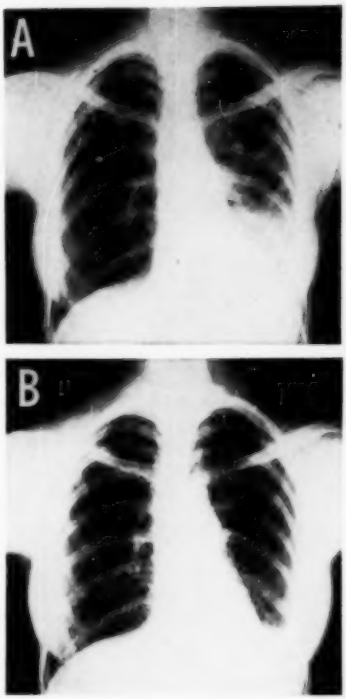


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DISEASES *of the* CHEST

VOL. XVIII SEPTEMBER 1950 NUMBER 3

# Early Detection of Bronchogenic Carcinoma

ROBERT R. SHAW, M.D., F.C.C.P.*
Dallas, Texas

Sixteen years have now passed since Graham first successfully removed a total lung for bronchogenic carcinoma. Following this initial success other surgeons soon reported successful resections of lungs for carcinoma. In spite of the fact that the early mortality was above 50 per cent, surgical extirpation of the disease did introduce a ray of hope in the otherwise dismal picture of cancer of the lung. Improvements in methods of anesthesia, adequate blood replacement, and improved surgical technique in the handling of the hilus of the lung have reduced the mortality to less than 10 per cent. This improvement in mortality has been accomplished in spite of the fact that the indications for operability have been extended. It has now been found technically feasible to not only remove the lung but also remove a portion of the chest wall, the diaphragm, and the pericardium when the neoplasm has extended to these structures.

The overall salvage rate in bronchogenic carcinoma still remains disappointingly low. Far too many patients presented to the thoracic surgeon are in too far advanced a stage of their disease to permit surgical removal of the neoplasm. Recently we have surveyed our experience for the past three years with 210 patients having bronchogenic carcinoma. We found that 50 per cent of the patients were obviously inoperable when seen by us either because of extension of the carcinoma to other portions of the body, the poor general condition of the patient, or invasion of the carcinoma within the chest so as to preclude the possibility of a successful resection. In the remaining 50 per cent where it was thought that surgery offered a reasonable chance of either effecting a cure or of palliation, it was found impossible to carry out a resection in half of these patients. This means that only 25 per cent of the

*Associate Professor of Thoracic Surgery, Southwestern Medical College, Dallas, Texas.

original group were suitable for surgical resection of their tumor. In a portion of this 25 per cent only palliation was being attempted since there was no chance of complete cure. There were five deaths in the 72 resections, a mortality of 6 per cent. In view of the age group of the patients and the technical difficulties at times encountered in attempting resection, it is not believed that the mortality of resection for carcinoma can be appreciably reduced. The only hope, therefore, in improving the overall results in the surgical treatment of this disease is in its early detection.

A review of the history of these patients showed that there was a delay of approximately five months between the time that the patient first experienced symptoms of the disease and his first visit to a physician. This delay will be a difficult one to eliminate. It may be that through education of the public as to the significance of changes in a cough history and of the spitting up of blood, patients may present themselves earlier to physicians and an earlier diagnosis can be made. More significant, however, was the delay between the time the patient presented himself to the physician and of making a correct diagnosis. An average of six months was consumed in making an accurate diagnosis in this group. The responsibility for this six months' delay is that of the medical profession and is one that we should try hard to eliminate. It has been estimated that for each month delay following the diagnosis of bronchogenic carcinoma in an apparently operable state the patient loses approximately 25 per cent of his chance of obtaining eventual cure. Neoplasm is an advancing disease and although there may be various rates of growth, no one can predict at just what time a blood borne metastasis may go to a distant organ or when the lymphatic extension to the nodes of the mediastinum may become so extensive that surgical extirpation is impossible. Bronchogenic carcinoma once diagnosed should be treated as an urgent surgical problem and all other factors in the patient's situation should be considered secondary to its treatment. Attempts to improve the patient's condition generally for surgery are not rational in that it is impossible to build up the patients against the ravages of this disease. Any time lost in this building up process may actually deny the patient his chance to be cured because of some distant extension of the disease.

What are the reasons for this six months' delay between the time the patient presents himself to the physician and the time an accurate diagnosis is made? It certainly is not a lack on the part of the physician in his concern for his patient. In almost every instance the delay is due to an original error in diagnosis. The diagnoses most often made in the early case of bronchogenic carcinoma are asthma, bronchitis, unresolved pneumonia, virus

pneumonia, tuberculosis, and fungus diseases. Attitudes of mind may contribute to the early delay in diagnosis. Physicians as a whole are not sufficiently aware of the prevalence of this disease. Bronchogenic carcinoma has now become one of the most frequent neoplasms encountered at the autopsy table. It is the most common carcinoma as a cause of death in males. If the prevalence of this condition is kept in mind especially in the age group above 40, many more of these patients having this condition will come to early diagnosis. There is also a natural reluctance to make a diagnosis of a disease that carries a high mortality. This reluctance should give way to an eagerness on the part of the physician to detect these neoplasms early when cure is still possible. Many physicians have gained their conception of the pathology of this disease from autopsy table so that they do not think in terms of early cell changes in the bronchial mucosa causing an obstruction of a small branch bronchus without obvious tumor formation.

Virus pneumonia and unresolved pneumonia are two diagnoses which are frequently made that contribute to the delay in diagnosis of bronchogenic carcinoma. The diagnosis of virus pneumonia is frequently made on flimsy evidence. There is no positive diagnostic test for this condition. The diagnosis can only be made after other conditions which may simulate virus pneumonia have been completely ruled out. If a diagnosis of virus pneumonia is made and the lesion within the chest does not clear promptly, as a lesion of virus pneumonia should, the physician must immediately realize that an error in diagnosis has been made and that neoplasm is to be considered. Virus pneumonia accounted for more than 50 per cent of the errors in diagnosis in patients having bronchogenic carcinoma that were finally referred to us for treatment. Persisting in this diagnosis often caused a delay beyond the time when it was possible to do anything for the patient surgically.

Unresolved pneumonia, a common diagnosis in the past, now in view of a better understanding of pulmonary lesions should be discarded. This is a diagnosis made from roentgen examination of the chest to describe a shadow of unknown origin. Pathologists do not recognize it as a pathological entity. The term they use in describing a pulmonary lesion producing such a shadow is fibroid pneumonitis which usually occurs beyond a blocked bronchus. The block may be due to neoplasm. True pneumococcal pneumonia will resolve by resolution and if a shadow persists more than two weeks after the initial onset of the disease an error has been made in diagnosis. Tuberculosis, pulmonary abscess, pneumonitis surrounding bronchiectasis, primary bronchogenic carcinoma, and fungus disease of the lung are the common conditions that have

been mistakenly called unresolved pneumonia. The fact that a lesion has not resolved means that it was not a true pneumonia. The failure of resolution should prompt the physician to make a more accurate diagnosis.

Bronchogenic carcinoma starts with a piling up of cells in the bronchial mucosa. In its beginning it is entirely intraluminary. Thickening of the bronchial mucosa due to neoplastic changes in the cells will cause an obstruction of the bronchus which may allow an infection to be set up in the segment beyond the branch bronchus. The carcinoma at this time may be so small in size that it cannot be detected on the x-ray film. It is the pneumonitis beyond the blocking tumor that calls attention to he fact tha something is wrong within the lung. At times a careful and even repeated search for the neoplasm will be necessary even after the lung has been removed for bronchogenic carcinoma. The prosector is often impressed by the fibroid pneumonitis in the lung and entirely misses the small stenotic bronchus which has been occluded by the neoplastic tissue arising in the mucosa. It may be several months before the neoplasm breaks through the bronchial wall and expands into the pulmonary tissue to a sufficient size to cause an x-ray shadow denoting its presence. In squamous cell carcinoma which is the type of malignancy that has the slowest growth potential and is thus the type that can most often be helped by surgery, its gradual extension may take place over a period of years. Recently I observed a patient who had an extremely early bronchogenic carcinoma in the lingular branch of the left upper lobe. Fortunately the carcinoma could be seen by bronchoscopy and a small bit was removed for pathologic study giving a positive diagnosis. The removal of the bit of carcinoma so improved the drainage of the segment which was blocked that the patient received immediate symptomatic relief and in spite of the fact that he was told that he had a neoplasm which would undoubtedly cause his death, he refused to have the lung removed. It was almost a year before the lesion caused sufficient trouble to prompt him to have anything further done about it. At this time he did consent to have x-ray therapy. The tumor gradually extended to block the entire lung but it was three years and four months following the diagnosis of the tumor before the patient finally succumbed to his disease. This case illustrates how long the process may go on before death ensues. In many patients even with small bronchial tumors it is possible to determine by history that the lesion undoubtedly was present for a year or more.

The diagnosis of bronchogenic carcinoma is made by a careful correlation of the history, laboratory findings, roentgen inspection of the chest, bronchoscopy if indicated, and exploratory thora-

cotomy. Examination of pleural fluid and biopsy of metastatic nodes, are not pertinent to this discussion since they are procedures used to diagnose an advanced stage of the disease. Needle biopsy of the pulmonary tumors is also not to be recommended as a means of early diagnosis since it might introduce complications which would make surgery difficult.

The history of the symptoms may be sufficient when considered in view of the x-ray appearance of the chest to give a clinical diagnosis of bronchogenic carcinoma. Even in the presence of an apparently negative examination of the chest the history alone may make one extremely suspicious that a neoplasm is present in the bronchi. Neoplasms in the left lung behind the heart shadow and those entirely intrabronchial may not cast shadows that can be easily seen and thus may escape detection on the average x-ray film. The early symptoms of bronchogenic carcinoma are: wheeze, cough, and the expectoration of blood streaked sputum. Such symptoms as pain, dyspnea, fatigue and weight loss are all symptoms of advance stage of the disease.

A localized wheeze may be the only symptom present in the early stage of bronchial neoplasm. The roentgen film of the chest may show a region of localized emphysema but this finding although highly significant is usually overlooked. Later infection causing a low grade fever will occur. Chemotherapy may cause symptomatic relief of the cough and fever and there may be an actual clearing of the shadow in the lung field. The physician should not conclude by this clearing that a neoplasm is not present. Incomplete clearing or the prompt recurrence of the infection in the same or neighboring segments of the lobe is highly suggestive of bronchial neoplasm even though no tumor mass can be seen. Although further studies do not prove the presence of a carcinoma, exploratory thoracotomy should be carried out.

Cough as a symptom may be difficult to evaluate. It is a common symptom with many diseases within the chest. Patients having early bronchogenic carcinoma usually give a history of having had a hacking cough ascribed to smoking which may have been present for many years. It is the change in the normal cough habit of the particular individual that should make one suspicious that a neoplasm has started in one of the bronchi. Paroxysms of coughing as if the person is trying to expectorate a foreign body is a significant type of cough.

The cough is usually non-productive although occasionally small bits of tenacious mucous may be expectorated. Blood streaks and blood clots may be seen in this mucoid material. The daily recurrence of blood in the sputum is highly suggestive of bronchial neoplasm. Severe hemorrhages may occasionally occur with bron-

chial carcinoma but this is exceptional. Frank hemoptyses are common in the presence of bronchial adenomas—a clinical benign tumor.

Laboratory examinations may indicate that the symptoms are due to another disease. Any sputum expectorated by the patient should be carefully examined for tubercle bacilli, predominating pyogenic organisms, and fungi. A positive laboratory report for any of these organisms should, however, be correlated with the history and with the appearance of the x-ray films since any one of these conditions may be present in addition to bronchogenic carcinoma. It was formerly thought that bronchogenic carcinoma was not common in patients having pulmonary tuberculosis. It is now realized that it is present in the same ratio as with people who do not have tuberculosis. The finding of fungi in the sputum may or may not be significant. Actinomyses, monilia albicans and even blastomyses are fairly common secondary invaders in bronchial secretions from pulmonary lesions. Their presence must not be accepted as evidence that these organisms are causing the condition unless it is felt certain that bronchogenic carcinoma has been eliminated as a possibility.

The extensive use of sensitivity skin tests has often caused confusion and delay in the diagnosis of bronchogenic carcinoma. It must be realized that these tests are only diagnostic aids and are not specific in themselves. The fact that a skin test is positive for coccidioidal mycosis does not mean that the shadow seen in the lung field is a coccidioidal granuloma. A positive tuberculin test is of no significance whatever in a patient having a shadow within the chest which could be a neoplasm. These skin tests at best can only lend supporting evidence and must never be considered diagnostic in themselves.

English observers many years ago pointed out the value of the examination of sputum with Wright stain for neoplastic cells. Lately the staining methods of Papanicolaou have revived interest in this subject. The clinical value of this examination depends much upon the experience of the personnel performing it. In some clinics as high as 85 per cent positive diagnosis of bronchogenic carcinoma are made by this method. It is not always necessary to collect bronchial secretions by bronchoscopy in order to make a diagnosis in this manner. Often by carefully selecting material coughed up by the patient, neoplastic cells can be demonstrated by these staining methods. It is important to train technicians to select material which contains dots of blood or blood streaks. The blood has come directly from the neoplasm and is more likely to have carried with it a few neoplastic cells. The finding of such cells in the sputum although it may clinch

the diagnosis does not make a bronchoscopy unnecessary since it will be important to make certain observations at the time of bronchoscopy to indicate whether or not thoracotomy should be carried out.

X-ray inspection of the chest using both posterior-anterior and lateral films is the most valuable diagnostic method that we have in investigating a patient who may have an early bronchogenic carcinoma. The neoplasm itself may not be visualized but the effect of the neoplasm in blocking the bronchus may give rise to shadows which are obvious. The pattern of these shadows in being limited to a lobe or to a segment of a lobe is highly suggestive of a block in a bronchus with suppuration beyond. The lateral film should always be taken along with the posterior-anterior film since there are fairly large regions in the lung fields that are not visualized by the ordinary posterior-anterior film. Small neoplasms can be obscured by the heart shadow. Since neoplasms tend to be in the major bronchi situated in the root of the lung it may be hard to interpret small changes in this region because of the presence of large vessels and lymph nodes. The lateral film will enable one to visualize many of these obscure areas. Especially significant is the small sharply circumscribed mass which may lie directly in the hilar area within the arch of the aorta as shown on the lateral film. This is highly suggestive of a neoplasm and if the clinical history supports may be sufficient to make an absolute diagnosis. In many patients an x-ray film of the chest after instilling iodized oil into the tracheobronchial tree will yield valuable information. An abrupt block of a bronchus or the tapering of a branch bronchus as shown by the oil filling may lend further support to a diagnosis of a bronchial neoplasm. One must always keen in mind in the study of x-ray films that we are interpreting shadows and that there is nothing diagnostic about the type of shadow cast by bronchogenic carcinoma. Interpretation of the shadow must be made in correlation with the history, the physical signs, the laboratory tests, and findings at bronchoscopy.

Mass x-ray surveys may bring to light bronchogenic carcinomas which are still in the asymptomatic stage. These are usually the small peripheral neoplastic masses which have not yet caused irritation of a major bronchus. Every sharply circumscribed abnormal shadow within the lung fields should be treated with extreme suspicion. It is true that many other lesions may simulate the appearance of neoplasm and may be of a type which will not harm the patient. Nevertheless the chance that the lesion is malignant is so good that exploration should be recommended when such a shadow is found. X-ray surveys have definite limita-

tions, however, in the early detection of bronchogenic carcinoma. It is not feasible to repeat these surveys at frequent intervals at the present time. Due to this fact, a person with a perfectly negative x-ray film at one period of time may develop bronchogenic carcinoma a few months later. This neoplasm will probably not be discovered until the patient has reached a symptomatic stage since he has already been assured that the chest is not the site of disease. It is also possible that the survey film may not show a very early carcinoma if suppuration has not occurred beyond the blocking tumor. In the future it may be possible to take yearly x-ray films on everyone who has passed the age of 40. Routine periodic x-ray surveys of this sort should undoubtedly bring to light many more bronchogenic carcinomas in a curable state.

Bronchoscopy is a valuable procedure in both the diagnosis of the bronchogenic carcinoma and in the evaluation of the patient from the standpoint of operability. It must be remembered that all parts of the bronchial tree are not visible by bronchoscopy. This means that many carcinomas arising in the periphery of the lung or in the second order branch bronchi of the lower lobes and in the first order bronchi of the upper lobes are not accessible to biopsy through the bronchoscopic route. It is true that the aspiration of secretions during the time of bronchoscopy may give material which upon examination will show malignant cells. Failure to find these cells, however, does not rule out carcinoma. In view of the limitations of bronchoscopy in examining the tracheobronchial tree it must be remembered that a negative result does not mean that carcinoma is absent. Bronchoscopy, should, however, be done routinely before contemplating surgery since it can yield very valuable information even if the tumor cannot be seen. At times at bronchoscopy it may be found that the shadow seen in the x-ray film does not comprise all of the tumor within the lungs. Occasionally the shadow seen upon x-ray films may be peripheral and yet there may be gross involvement of the bronchi in the region of the bifurcation of the trachea. In the very early bronchogenic carcinoma bronchoscopy becomes less valuable. In less than half of the patients diagnosed in an early stage of their disease will it be possible to see the tumor. In many patients the clinical history is so strongly suggestive that exploration of the chest is advisable in spite of negative bronchoscopic findings.

Exploratory thoracotomy has now become so safe that it can be recommended even in the absence of a positive pathological diagnosis of bronchogenic carcinoma. At the time the chest is opened the lung can be palpated and specimens removed for pathologic study by frozen section if this seems desirable. It must be admitted

that even at the time the chest is opened it is often difficult to make an absolute diagnosis of bronchogenic carcinoma. The trained observer, however, by palpating the root of the lung and the bronchial tree can usually detect changes in the bronchi which are indicative of bronchogenic carcinoma.

The passage of time is not on the side of the patient who has a bronchogenic carcinoma. For this reason it is unwise to advise a patient to wait for a specified period of time to see what will happen to symptoms or to an unexplained shadow which has appeared in the x-ray film. Nearly always the period of waiting extends past the time that anything can be done for the patient with surgery. If there is any suspicion of bronchial carcinoma the patient deserves to have an exhaustive study in an attempt to make an accurate diagnosis. There are times when after a careful study there does not seem to be sufficient evidence to warrant advising an exploration of the chest. In this circumstance, a period of close observation can be advised with repetition of the diagnostic studies that seem advisable if the symptoms do not improve and the shadow as seen by x-ray film does not completely disappear. In some cases it may be necessary to honestly tell the patient the condition that is being suspected in order to gain his complete cooperation. Time is the essence of success in surgical treatment of bronchogenic carcinoma. Although it is true that bronchial carcinomas extend at different rates in various individuals, the extension is inexorable and for that reason the passage of time is working continually against the patient.

Unfortunately there is a large group of patients having bronchogenic carcinoma in which it is impossible to make a diagnosis in a state where surgery can offer any chance of cure. In studying our patients we found that in 25 per cent the initial complaint which prompted the patient to consult his physician was one which indicated inoperability. Headaches due to cerebral metastasis, loss of voice due to involvement of the recurrent laryngeal nerve, painless pleural effusion which caused only shortness of breath, difficulty in swallowing due to involvement of the esophagus, and skin metastases indicating generalization of the neoplasm are rather common initial complaints which prompt the patient to visit his physician. All of them indicate inoperability. Pain may not indicate absolute inoperability but is usually a sign of poor prognostic significance since it may mean extension of the tumor beyond the lung to some parietal structure. We also found that approximately 20 per cent of our patients had undifferentiated bronchogenic carcinoma. One of this pathological type is highly invasive and tends to metastasize early through the blood stream to different parts of the body. There has been only one question-

able five year cure for this type of carcinoma reported in the literature. It has come to be recognized that an undifferentiated bronchogenic carcinoma should probably be considered a sign of inoperability. If we add the 25 per cent whom the initial complaint indicated inoperability to the 20 per cent who have the undifferentiated type and allow for some over-lapping in the two groups we estimate that 40 per cent of patients having bronchogenic carcinoma are inoperable at the time they are first seen by their physician. This leaves un only 60 per cent of patients in whom an early diagnosis may make a cure possible. These statistics are not quoted to add discouragement to the problem of bronchogenic carcinoma but only to point out the difficulties which confront the practitioner and the thoracic surgeon in dealing with this disease.

Intelligent observation by a patient of personal habits and the alertness of a physician may "pay off" in the early diagnosis of bronchogenic carcinoma. This is well illustrated by a patient seen by me over four years ago. A 64 year old woman who otherwise was in perfect health noticed that for every morning of the previous three weeks she had cleared her throat and raised some mucoid material which contained small blood streaks. This was an abnormal occurrence for her. She immediately consulted her personal physician who made x-ray film inspection of her chest which showed a small sharply circumscribed shadow in the left upper lobe in the anterior portion of the chest. Examination of the sputum revealed no significant organisms. The woman had no fever, did not feel tired, and had no pain. Six years previously she had a carcinoma of the cervix which also had caused minimal bleeding and was detected early. This carcinoma was treated by radium therapy and frequent examinations of the pelvis had failed to reveal any further evidence of neoplasm. Thoracotomy was advised to determine the nature of the lesion within the left lung and the patient readily agreed. Upon opening the chest a small hard lesion was felt in the anterior segment of the left upper lobe. It was not adherent to the parietal pleura but there was a small reddened area where the lesion had been in contact with the parietal pleura. The parietal pleura over this region was widely excised. Examination of the hilum of the lung failed to reveal enlarged lymph nodes. The segmental bronchus and artery were isolated and divided and the segment of the lung was stripped from the remaining portion of the lobe. Pathological examination of the specimen revealed it to be a grade I, squamous cell carcinoma which had undergone central necrosis accounting for the expectoration of the blood streaked sputum. The woman made an uneventful recovery from surgery. She has remained entirely well

to the present date. The intelligence of the patient and the alertness of the physician has contributed to prolongation of this woman's life with a minimal sacrifice of pulmonary tissue. It is not often that one is going to be so fortunate to find a case as early as this one but continued vigilance on the part of the general practitioner and insistence upon accurate diagnoses of lesions appearing within the lung will bring more and more patients having bronchogenic carcinoma to the thoracic surgeon at a stage where the lesion can be completely removed.

## SUMMARY

1) In spite of the fact that the mortality of pulmonary resection for bronchogenic carcinoma is now less than 10 per cent, the salvage of patients having this disease is still disappointingly low. Earlier diagnosis is our only means of improving this salvage.

2) In our experience there is a five months' delay between the onset of symptoms and the time the patient presents himself to the physician and a further delay of six months between the visit to the physician and a correct diagnosis.

3) The delay in correct diagnosis is usually due to the making of an incorrect diagnosis. Virus pneumonia and unresolved pneumonia are two diagnoses that are frequently made in patients having this disease.

4) The early bronchogenic carcinoma represents only a change in the bronchial mucosa which obstructs the bronchus. Signs or symptoms of bronchial obstruction should be regarded with suspicion. A localized wheeze and the finding of a region of localized emphysema on the x-ray film are the earliest symptom and sign of bronchogenic carcinoma. Cough is the most common symptom complained of by the patient. In evaluating this symptom the change in the cough history from a hacking cough to paroxysmal type of coughing is the most important factor.

5) X-ray inspection of the chest is the most valuable diagnostic method in the detection of this disease. Mass radiography is bringing to light many early lesions in the asymptomatic stage. Mass radiography, however, unless repeated often cannot be the answer to early diagnosis.

6) Bronchoscopy is an excellent diagnostic procedure but when negative does not rule out bronchogenic carcinoma. The examination for neoplastic cells in material coughed up or obtained at bronchoscopy has made it possible to make many more early diagnoses.

7) Exploratory thoracotomy may often be necessary in order to

diagnose early bronchogenic carcinoma. Exploratory thoracotomy is safe and should be recommended when there is sufficient evidence to suspect early neoplasm.

8) In our patients it was found that approximately 40 per cent were inoperable at the time they first visited the physician. This disappointing fact is one reason why the salvage rate in this disease is still low.

9) Continued vigilance on the part of the general practitioner and insistence upon accurate diagnoses of lesions appearing within the lung will bring many more patients having bronchogenic carcinoma to the thoracic surgeon at a stage where the lesion can be completely removed.

## RESUMEN

1) A pesar de que la mortalidad en la resección pulmonar, por cáncer broncogénico es ahora por debajo del 10 por ciento, la cantidad de enfermos curados es todavía muy pequeña.

2) En nuestra experiencia, hay un período de cinco meses de espera, desde el comienzo de los síntomas hasta que el enfermo es visto por un médico; y después otra espera adicional de seis meses hasta que el diagnóstico correcto se ha hecho.

3) Generalmente la tardanza en el diagnóstico correcto es debida al hecho de que se ha hecho un diagnóstico incorrecto. Pneumonia a virus filtrable, o pneumonia no resuelta, son dos diagnósticos que se hacen frecuentemente en enfermos con esta enfermedad.

4) El cáncer broncogénico, al principio presenta solamente un cambio en la mucosa bronquial, la cual obstruje el bronquio. Signos y síntomas de obstrución bronquial, deben ser considerados sospechosos. Un roncus localizado y una región de enfisema localizado en la radiografía, son los primeros signos y síntomas del cáncer broncogénico. La tos, es el síntoma mas común. Un factor importante en este síntoma, es cuando cambia, desde una tos seca, a una tos paroxística.

5) El exámen radiográfico, es el metodo mas importante en el diagnóstico precoz de la enfermedad. Radiografía en masa, de la población, es un factor muy importante en los casos que todavía no presenten ningún síntoma.

6) La broncoscopía es un medio de diagnóstico excelente, pero cuando es negativa pierde su valor. El exámen citológico de los esputos o de los lavados bronquiales, ha hecho posible muchos diagnósticos precoces.

7) Toracotomía exploradora, frecuentemente es necesaria para

hacer un diagnóstico precoz de carcinoma broncogénico. La toracotomia exploradora no presenta ningún peligro y debe ser recomendada siempre que haya evidencia suficiente de una sospecha de neoplasma precoz.

8) En nuestra serie, hemos encontrado que aproximadamente 40 por ciento eran inoperables en la primer visita médica. Este hecho triste, es una de las razones del porque, el porcentaje de curas es tan pequeño.

9) Vigilancia continua de parte del médico práctico, un diagnóstico mas preciso de las lesiones pulmonares, traera mas enfermos con cáncer broncogénico a la atención del cirujano del tórax, en un momento cuando la lesion puede ser extirpada completamente.

# Sarcoidosis

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Sarcoidosis is a chronic systemic granulomatous disease of unknown etiology with clinical findings so benign they appear unrelated to the widespread lesions which usually are found on physical and laboratory examination. The exact incidence of the disease is unknown, although the number of reported cases has increased greatly in the past few years. This may be due to the widened interest in sarcoidosis, and consequent sharpened diagnostic acumen, or less likely to an augmented incidence of the disease. A growing interest has been evidenced in the United States largely since 1937.[1-7] Two excellent reviews of the subject have been published recently by Freiman[8] and Curtis and Grekin.[9]

At the University of California Hospital, only seven cases were classified under any of the synonyms of sarcoidosis prior to 1937. Since then, in a census approximating 165,000 clinic and hospital admissions, only 28 cases were recorded. Investigation of material at the San Francisco Hospital shows essentially comparable findings. However, examination of cases diagnosed as "Boeck's Sarcoid" discloses variations in the studies performed, which make the final diagnosis doubtful in a number of the cases. It is the purpose of this paper to review the difficulties encountered in the diagnosis of sarcoidosis in an attempt to clarify a needed approach to the basic understanding of the disease process.

The disease was described first by Hutchinson[10] in 1875, by Besnier[11] in 1889 as lupus pernio, and in 1899 by Boeck[12] as multiple benign sarcoids of the skin. Heerfordt[13] in 1909 reported uveoparotid fever, now considered a characteristic symptom complex of the disease. Jungling in 1919[14] described the bone lesions under the name ostitis tuberculosa multiplex cystica, revising the name in 1928[15] to ostitis tuberculosa multiplex cystoides. Schaumann[16] in 1916 related lupus pernio, sarcoidosis, and tuberculosis, and shortly thereafter considered all the lesions as part of a systemic disease under the term lymphogranulomatosus benigna. Nickerson[17] in his review of six necropsied patients in 1937, was the first to report lesions in the myocardium, endocardium, pancreas, testis, and vertebral and femoral marrow. In 1937, Long-

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cope and Pierson[1] showed the chronic granulomatous nature of the disease. Pinner[2] in a review of the existing material in 1938, used the phrase "non-caseating tuberculosis." Since that time, the most important studies have attempted to (1) clarify the etiology and life history of the disease and (2) to develop specific tests for the diagnosis of sarcoidosis.

*Etiology:* The etiology of sarcoidosis remains unknown. At the present time, according to several definite schools of thought, the causative factor is thought to be: (A) tuberculosis,[2,18-23] (B) leprosy,[24,25] (C) chronic granuloma of unknown or varied etiology,[1,6] (D) fungus,[26] and (E) a variety of others.[5,27,28] Recent work,[29-34] in relation to specific diagnostic tests based on Williams' and Nickerson's[28] earlier studies, gives some evidence that the etiology is specific.

*Pathology:* The pathology of the disease is well known.[1,5,17,35,36] The lesions consist of miliary tubercles composed of epithelioid cells, multinucleated giant cells, and a small scattering of peripheral lymphocytes. Minimal central necrosis may be present, but there is no caseation. The lesions may develop in the reticuloendothelial system at any location throughout the body. After the lesions heal, the scars generally appear atrophic, hyalinized, and fibrotic.

*Distribution of Lesions:* The organs most frequently involved are the skin, lymph nodes, bone, lungs, spleen, liver, uveal tracts, and parotids. More rarely, the peripheral nerves, nasal mucosa, pharynx, larynx, conjunctiva, myocardium, endocardium, pancreas, striated muscle, mammary glands, eyelids, knee joints, epididymis, and colon are implicated. There is no predominant distribution of skin lesions. Reisner[3] found the peripheral nodes involved in all of his patients. It is of interest that Schaumann[37] and others have noted a high percentage of cases of sarcoidosis in which lesions appear in the tonsils. Such figures have not been reported from the United States, probably because of the incidence of tonsillectomy in early life. Lesions in the lungs[3,36,38-44] are found commonly on roentgenographic inspection of the chest, either in diffuse miliary or nodular form with linear accentuation of bronchovascular markings, or as localized or widespread pneumonic infiltrations. Hilar lymph node involvement is frequent. The actual incidence of bone lesions is not known. According to Pinner,[2] this is partly because not all patients are examined roentgenographically, and partly because patients with such lesions have been described as having a separate disease without regard to associated lesions. However, certain authors[1,6,38-40] report that about 10 to 20 per cent of patients with sarcoidosis show roentgenographic evidence of lesions in the bones of the hands and

feet and, less often, in the long bones. The lesions appear as cystic areas of rarefaction due to invasion and destruction of the bone by the granuloma. Involvement in other organs which occurs more rarely has been reported in isolated cases or as a distinctly minor finding in large series.

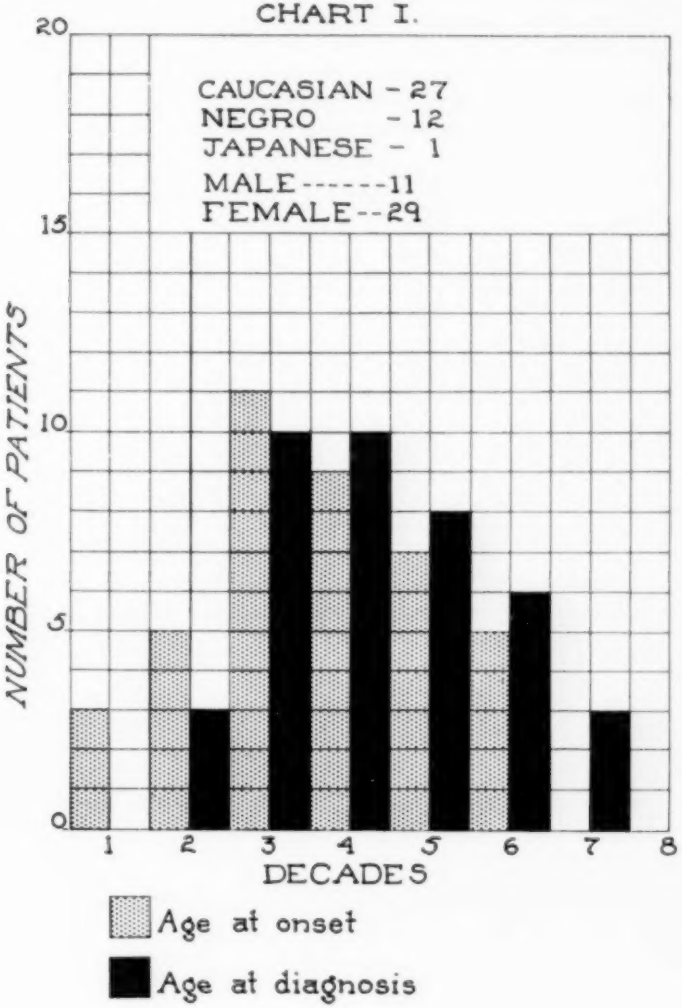
*Clinical Course:* Clinically, the disease is marked by a paucity of symptoms and a usually benign course. Many of the patients have histories of some years' duration suggestive of sarcoid, but consult a physician only after the development of overt and often unpleasant lesions.

The patients may complain of skin lesions, lymph node swelling, slight dyspnea or cough, eye changes, and, more rarely, of the soft tissue swelling and generally fusiform appearance of fingers and toes associated with the bone disease.

On physical examination, the findings in each case are restricted to the organs involved. There may be a variety of skin lesions, ranging from sharply circumscribed papular or raised nodules to diffuse, purplish or red areas, either raised or flat, of variable distribution. Involvement of the external lymph nodes is common. The nodes are generally of firm consistency, non-tender, of variable size, freely moveable, and not matted. Findings in the lungs vary with the degree of parenchymal involvement and the amount of pressure exerted on surrounding tissues by hilar and paratracheal nodes. The heart may be involved. Commonly, there is an absence of clinical findings; the abnormalities are revealed only in electrocardiograms. The changes generally indicate interference with the conduction mechanism or myocardial involvement. In some patients, there is increased right heart pressure secondary to pulmonary lesions with mechanical obstruction of the pulmonary vascular structures. The spleen and liver are often palpable. The bone lesions are not necessarily accompanied by pain; in some instances, there is visible local swelling or a fusiform deformity. Many bone lesions are found only because there is suspicion of sarcoidosis and appropriate x-ray films are taken.

The diagnosis is based upon the benign course, physical findings, chest or bone roentgenograms, and, most unequivocally, biopsy specimens showing the characteristic lesions. An elevated serum globulin is of aid but is not diagnostic. The erythrocyte sedimentation rate may or may not be elevated. At times, a moderate eosinophilia or monocytosis is present. Generally, the sternal bone marrow shows only irritation such as is found in chronic infections.[45] The Kveim reaction is said to be a specific test for the disease, but as has been pointed out by Lomholt[31] and Putkonen,[33] there may be delayed necrotic reactions at the point of injection; also, there is some doubt that the test is specific

(Danbolt[46]). A negative tuberculin test is helpful but not diagnostic, as there is an anergy[2] in only about 70 per cent of the cases. Lemming,[47] and later Forsmann,[19] have used the BCG vaccination to prove the presence or absence of sarcoidosis. They find typical lesions, demonstrable on biopsy, will develop as the site of vaccination on patients with sarcoidosis but not on patients with tuberculosis or other conditions. Also, the negative reaction



to tuberculin will not become positive after BCG vaccination in patients with sarcoidosis. There may be a falsely positive serologic test for syphilis. Unless the kidneys are directly involved, there are no demonstrable changes on urinalysis. Other abnormalities, depending on changes in specific organs or systems, are found on laboratory examination.

*Material:* This series consists of 40 patients seen at the University of California Hospital and the San Francisco Hospital (Chart 1). These patients were followed intermittently by various clinicians for as long as 12 years (one for 30 years). There were 29 females and 11 males; 27 were white, 12 were Negro and one was Japanese. The patients were classified as to age at diagnosis and probable age at onset as determined by history. The majority of patients, 28 (70 per cent), were between the ages of 20 and 50; 10 (25 per cent) were between 20 and 29; the youngest was 11. The probable age at onset was slightly younger, 25 (63 per cent) between the ages of 10 and 40; 11 (27.5 per cent) between 20 and 29, and the youngest at the age of four. Detailed studies of the group were too incomplete to permit any evaluation of course and prognosis. In the three patients known to have been necropsied, the diagnoses were periarteritis nodosa in a chronic granuloma of unknown etiology, miliary tuberculosis, and disseminated tuberculosis with coincident undiagnosed carcinoma of the stomach, respectively.

*Coexisting Diseases:* An attempt was made to analyze the coexisting diseases found in these patients, and if possible, to correlate them with sarcoidosis. No such relationship was found. The coexisting diseases were present no more frequently than in the general clinic population, and no particular disease could be singled out as occurring predominantly.

*Initial Clinical Diagnosis:* The "initial clinical diagnoses," those made before x-ray, biopsy, or other significant studies were reported, were of interest (Table 1). Sarcoidosis was thought of initially in 15 cases; "lymphoma" was considered in 15 (with Hodgkin's disease named specifically in many of these); pulmonary tuberculosis in 12; coccidiodomycosis in five; and syphilis in five.

Considered by systems and organs, the following was observed: Pulmonary symptoms and findings led to the consideration of tuberculosis, pneumonia, bronchial asthma, pneumoconiosis, pulmonary fibrosis, bronchiectasis, tumor, and lung cysts. The findings were so bizarre they gave rise to serious consideration of a psychogenic disorder in two patients, and a pituitary lesion with acromegaly in one. Ocular abnormalities warranted an initial clinical diagnosis of 18 types of lesions. Granulomatous involve-

ment of the nasal mucosa led to consideration of a nasal malignancy in one patient. Findings related to the heart were remarkably few. The gastro-intestinal and genito-urinary systems were of little help in establishing an initial diagnosis. Four patients were classified initially as having "erythema nodosum," and one "erythema multiforme." Because five patients presented central nervous system manifestations, the diagnoses of nerve palsies, poliomyolitis, encephalomyelitis, subdural hematoma, and brain tumor were considered. Also mentioned initially were systemic infections, such as brucellosis, tularemia, moniliasis, infectious mononucleosis, trichinosis, malaria and others.

Thus, it was found that the systems most frequently implicated in making a diagnosis were the pulmonary, reticulo-endothelial, head and its appendages, and the neuromuscular. It is evident that the differential diagnosis covered a wide range of diseases. Predominantly considered were sarcoidosis, tuberculosis, Hodgkin's disease, coccidiodomycosis, syphilis, and other chronic infections of varying nature.

*Final Clinical Diagnosis:* The final clinical diagnosis was sarcoidosis in 36 cases. Of the other four, three remained unclassified, and at necropsy one was found to be miliary tuberculosis. There was a total of 30 other diagnoses, but these were divisions of the basic classification to show organ involvement and secondary

TABLE I

Initial Clinical Diagnoses (By Systems and Diseases)

| | | |
|---|---|---|
| Systemic Infections and Diseases | 55 | |
| Sarcoidosis | | 15 |
| Head, Eyes, Ears, Nose, Throat | 25 | |
| Pulmonary | 21 | |
| Tuberculosis | | 12 |
| Reticulo-Endothelial System | 22 | |
| Lymphoma | | 16 |
| Neuromuscular | 18 | |
| Integument | 11 | |
| Cardio-Vascular | 8 | |
| Genito-Urinary | 5 | |
| Gastro-Intestinal | 5 | |
| Unclassified | 6 | |
| TOTAL | 176 | |

features. Finally, in seven, an associated diagnosis of tuberculosis was made.

*X-Ray Diagnosis:* If any consultation service may be accredited with having suggested the diagnosis of sarcoid frequently, it was the Division of Radiology (Table 2). Chest x-ray films of 33 patients were made.

*Predominant Symptoms:* The predominant symptoms and complaints during the course of the illness were divided into several large groups (Table 3), which clearly showed the protean manifestations of sarcoidosis. Seventeen patients noted definite weight loss of five to 30 pounds in periods of varying duration; 10 were aware of fever; nine of night sweats; seven of increasing weakness; six of fever and chills; six of fatigability, and three of malaise. These complaints were found in a total of 29 patients. The remaining 11 had no complaints of a general systemic nature.

In the region comprising the head, eyes, nose, and throat, 21 patients complained of a total of 27 symptoms. Twelve of these were related to the eyes and six to the nose and throat. Nine patients complained of headaches of varying degree. The eye complaints included swelling, itching, burning, impaired vision, and inflammation. The nose and throat complaints were parotitis, exclusive of known mumps and sore throat, and a depression in the bridge of the nose.

Cardio-respiratory symptoms were present in 23 of the patients. Thirteen had cough of varying degree and type. Twelve complained of shortness of breath and "asthma," the duration varying from two months to 12 years. Eight had chest pain of no characteristic duration, location, or relation to respiration, cough, or exertion. Four had small hemoptysis. While the chest x-ray inspection in sarcoidosis offers findings indicative of widespread involvement, only 23 patients (57 per cent) were disturbed sufficiently by chest complaints to bring them to the clinician's attention.

TABLE 2

Roentgen—Diagnoses

| | |
|---|---|
| Pulmonary Tuberculosis | 15 |
| Sarcoidosis | 13 |
| Lymphoma | 9 |
| Pulmonary Mycoses | 7 |
| Non-Specific Infections (pulmonary) | 6 |
| Tumor (pulmonary, all types) | 4 |
| Cor Pulmonale | 2 |
| All others | 12 |

There were few complaints of disturbance of the gastro-intestinal system; five patients noted anorexia and three abdominal pain of no characteristic nature. Laparotomy was performed on one patient after several years of such pain, and typical lesions were found in nodes in the region of the pancreas. No patient had complaints referable to the genito-urinary system. Ten were disturbed by joint pains of varied description, few of which were related to the cystic bone lesions. Four complained of nerve symptoms generally, in the form of peripheral nerve palsies.

Lymph node enlargement was exceedingly uncommon as a symptom in this group. Tenderness was generally not a presenting complaint, and the patients were disturbed only by the increased size of the nodes. In one patient another element of the reticulo-endothelial system, the spleen, became enlarged sufficiently to be disturbing.

TABLE 3
Predominant Symptoms

| System | Symptom | Number |
|---|---|---|
| General | Weight loss | 17 |
| | Fever | 10 |
| | Night sweats | 9 |
| | Weakness | 7 |
| | Chills and Fever | 6 |
| | Fatigability | 6 |
| | Malaise | 3 |
| Head, Eyes, Nose, Throat | All eye complaints | 12 |
| | Headache | 9 |
| | All E-N-T complaints | 6 |
| Cardio-Respiratory | Cough | 13 |
| | Dyspnea and "Asthma" | 12 |
| | Chest pain | 8 |
| | Hemoptysis | 4 |
| Gastro-Intestinal | Anorexia | 5 |
| | Abdominal pain | 3 |
| Neuromuscular | Joint symptoms | 10 |
| | Neurological symptoms | 4 |
| Lymphadenopathy | | 5 |
| Cutaneous Lesions | | 13 |
| Loss of tissue (i.e.: Saddle Nose) | | 1 |

Thirteen of the patients were sufficiently disturbed by skin lesions to come to the clinic. These lesions were variable in nature; some were ecchymotic areas, others tiny intracutaneous nodules, and still others plaques of variable shape and size. One patient

TABLE 4

Physical Findings

| | Total No. of Patients | No. of Individual Findings | Per cent of Total (40) |
|---|---|---|---|
| Skin Lesions | 24 | | 60 |
| Nodules | | 18 | 45 |
| Psoriasiform lesions | | 6 | 15 |
| Indurated areas | | 4 | 10 |
| Ecchymotic areas | | 2 | 5 |
| More than one type | | 4 | 10 |
| Palpable Lymph Nodes (peripheral) | 28 | | 70 |
| Cervical | | 22 | 55 |
| Inguinal | | 17 | 42.5 |
| Axillary | | 16 | 40 |
| Epitrochlear | | 10 | 25 |
| Mixture of types | | 19 | 47.5 |
| Ocular Lesions | 14 | | 35 |
| Conjunctivitis | | 8 | 20 |
| Uveitis | | 4 | 10 |
| Iritis | | 3 | 7.5 |
| Others | | 7 | 19.2 |
| Mixed lesions | | 5 | 12.5 |
| Parotid Lesions | 3 | | 7.5 |
| Right | | 1 | 2.5 |
| Bilateral | | 2 | 5 |
| Pulmonary Findings | 17 | | 42.5 |
| Cardiac Findings | 15 | | 37.5 |
| P2 (greater than) or = A2 | | 14 | 35 |
| Pericardial friction rub | | 2 | 5 |
| Palpable Spleen | 12 | | 30 |
| Palpable Liver | 16 | | 40 |
| Visible Bone Lesion (including clubbing) | 6 | | 15 |
| Neurologic Lesion (any type) | 4 | | 10 |

had a depression of the bridge of her nose, where a granuloma had completely destroyed the underlying tissues.

*Physical Examination:* Physical examination (Table 4) showed the skin involved in 24 of the patients, four of whom had two distinct types of lesions. Eighteen had subcutaneous nodules, single or multiple, six had psoriasiform lesions, four had areas of rough, red induration, and two had ecchymotic areas. There was no significant combination of lesions in the four patients with two types.

The external lymph nodes were involved in 28 of the patients. These nodes were classified arbitrarily as follows: cervical (22), inguinal (17), axillary (16), and epitrochlear (10). There was combined adenopathy in 19. As a rule the nodes, which were extremely variable in size, were firm, non-tender, freely moveable, and not matted.

The eyes were commonly affected. A total of 14 patients had an ocular lesion during the course of the disease, the majority (8) with conjunctivitis of varying degree. Four had an uveitis (but only one of these an associated parotitis), three had an iritis (one with an associated uveoparotitis), and seven exhibited other lesions, described as keratitis, glaucoma, and other ophthalmologic abnormalities. Five of the patients had a combination of conjunctivitis, uveitis, and iritis.

Parotitis, a relatively uncommon lesion, was unilateral in one patient and bilateral in two. A tuberculous etiology was established in one of the patients with a bilateral lesion.

Physical signs of pulmonary involvement were present in 17 patients. In association with these, cardiac findings were evaluated. Because of associated diseases related to the heart, the P2 - A2 relationship was considered only in patients above the age of 20. In no case was there recorded a change related to heart disease per se and in none was the patient in congestive failure. Fourteen had P2 louder than, or equal to, A2. Two presented a pericardial friction rub.

The spleen was palpable in 12 patients and the liver in 15. Visible bone deformaties in hands or feet were noted in six with clubbing in two. Four patients had some evidence of nerve weakness.

*Laboratory Findings:* (Table 5) Chest roentgenogram findings were divided into two large groups: those with parenchymal lesions and those with hilar node involvement. Of 33 patients examined, 24 had parenchymal changes of varying degree, and 17 had hilar node enlargement. There were combined lesions in seven. Five patients without peripheral adenopathy had x-ray evidence of hilar node disease. Thus a total of 33 patients had demonstrable lymphadenopathy. X-ray films of hands and/or feet were made

TABLE 5
Laboratory Examinations

| Examination | Total Examined | No. with Abnormal Findings | Per cent of Total Examined |
|---|---|---|---|
| Chest Film | 33 | | |
| Parenchymatous lesions | | 24 | 73 |
| Hilar adenopathy | | 17 | 51.5 |
| Combined parenchymal and nodal | | 7 | 21.2 |
| Hilar adenopathy without peripheral adenopathy | | 5 | 15.2 |
| Bone Films (all types) | 31 | | |
| Unequivocal lesions | | 4 | 12.9 |
| Questionable lesions | | 4 | 12.9 |
| Sputum Examinations* | 27 | | |
| Smear for acid fast bacilli | | 1 | 3.7 |
| Guinea Pig inoculations | | 1 | 3.7 |
| Cultures for acid fast bacilli | | 1 | 3.7 |
| Sputum Cultures for Fungi | 11 | | |
| Positive for *C. albicans* | | 4 | 36 |
| Skin Tests: | | | |
| Tuberculin (all dilutions)** | 32 | 9 | 28 |
| Coccidiodin | 23 | 0 | |
| Histoplasmin | 10 | 0 | |
| Frei | 3 | 0 | |
| Blood Tests: | | | |
| Kahn and Kolmer | 38 | 3† | 7.8 |
| Questionable | | 1 | 2.6 |
| White Blood Count | ?8 | | |
| 4000- 5000 | | 5 | 13.2 |
| 3000- 4000 | | 1 | 2.6 |
| 10000-12000 | | 2 | 5.2 |
| 12000-15000 | | 2 | 5.2 |
| over 15000 | | 2 | 5.2 |
| Eosinophils (over 5%) | 31 | 12 | 38.7 |
| Monocytes (over 10%) | 31 | 4 | 12.9 |
| Erythrocyte Sed. Rate†† | 27 | 17 | 63 |
| Elevated Globulin†† | 32 | 17 | 53 |

*Includes five with gastric washings.
**Three others were initially negative, later becoming positive, two shortly before death from tuberculosis.
†All three reverted to negative without adequate therapy.
††Elevated some time during the course.

on 31 patients, four of which revealed cystic changes characteristic of the disease, and four presented doubtful findings.

The sputum was examined in 27 cases. In 22, repeated smears and concentration technic tests for acid-fast bacilli were negative. Cultures of the sputum of 11 of the 22 patients were made on one or more media and were negative, as were guinea pig inoculations with the sputum of 13 patients. Smear, concentration, and guinea pig inoculation were all positive for acid-fast organisms in the sputum and pus of a parotid abscess in one of the patients.* In five cases, smears were examined for fungi and found negative. Cultures for fungi in 11 cases were reported positive for a "yeast" in one and for *Candida albicans* in four. Concomitant animal inoculation was not performed.

Tuberculin skin tests were performed on 32 of the patients. Seven of the tests were with Purified Protein Derivative (P.P.D.), of which four were negative and three positive with second strength PP..D. The remainder of the tests were made with Old Tuberculin (O.T.). Six were carried to 1:10 dilution, and all were negative. Seven others were carried to 1:100; of these, five were negative and two positive. Seven were tested with 1:1000 O.T.; of these four were negative and three positive. One was done with an unknown dilution, and was negative. One patient with a negative test (P.P.D. 2) had a skin lesion in which characteristic tubercles were demonstrated and in which acid-fast bacilli were found. Unfortunately, material from the lesion was not inoculated into a guinea pig. The patient was later vaccinated with BCG vaccine. Though a nodular lesion developed at the point of vaccination, she would not permit biopsy. Six weeks later, the tuberculin reaction (P.P.D. 2) was negative.

Serological tests for syphilis were negative in 34 patients. There were three with weakly positive tests which turned negative with inadequate or no treatment. One was strongly positive but later became weakly positive with inadequate treatment.

White blood cell counts done in 38 of the patients were below 5,000 cells per cubic millimeter in six cases (2,900 to 4,600) and significantly elevated in six (10,000 to 18,000). Eosinophilia of more than 5 per cent was found in 12 patients, only two of these associated with leucopenia and one with leucocytosis. Monocytosis of more than 10 per cent was found only four times, once associated with leucopenia. The erythrocyte sedimentation rate was elevated to a varying degree in 17 of the patients and normal in 10.

Serum albumin and globulin were determined in 32 patients; one determination was made in 20, two in seven, three in four,

*This patient was a proved case of sarcoidosis who later developed fatal disseminated tuberculosis. Case to be reported in detail elsewhere.

and four in one. The globulin was elevated above normal in 17 of the tested patients at some time during the course of the disease. The sternal marrow was examined in seven patients. Six showed a non-specific hyperplastic response and the seventh was normal.

Tissue biopsy is the single most important test to confirm the diagnosis of sarcoidosis (Table 6). Biopsies were made on tissue from 34 of the patients; of these, 29 were diagnosed as sarcoid. Skin biopsies in 17 and lymph node examinations in 13, were considered compatible with sarcoidosis. In four of these, both skin and lymph node were biopsied. In one patient, tonsillar tissue, and in another, pancreatic nodules removed at surgery were examined. Each showed characteristic tubercles. One specimen from a liver biopsy and splenectomy in the same patient showed sarcoid lesions. A section of peritonuem removed at laparotomy revealed sarcoid tubercles. Three skin biopsies were interpreted as consistent with tuberculosis, but acid-fast bacilli were found in only two. One lymph node was considered tuberculous, although no acid-fast organisms were demonstrated.

Bronchoscopy was normal in five patients with extensive intrathoracic involvement.

TABLE 6

Biopsies

| | | |
|---|---|---|
| Number of patients biopsied | 34 | |
| Number diagnosed as sarcoidosis* | 29 | |
| Skin and Lymph Nodes | | 4 |
| Skin | | 13 |
| Lymph Nodes | | 9 |
| Tonsil | | 1 |
| Spleen | | 1 |
| Liver | | 1 |
| Pancreatic Nodule | | 1 |
| Peritoneum | | 1 |
| Tuberculosis | 3 | |
| Skin | | 2 |
| Lymph Node | | 1 |
| Chronic perivascular dermatitis | 1 | |
| Atrophic Skin | 1 | |

*Multiple biopsies on several patients.

In six of nine patients on whom lumbar puncture was performed, there were normal findings. Of the remaining three, one had tuberculous meningitis. There was positive Pandy test and elevated protein in two.

Electrocardiograms were made in 20 cases. The records varied during the course in individual patients. One was interpreted as "borderline," of no characteristic pattern, and one month later was found to be normal, a finding which coincided with the diminished size of hilar nodes and pulmonary involvement. One was initially normal, but four years later revealed abnormal findings of no characteristic pattern. One was abnormal, of no characteristic pattern, but was never repeated. Of two showing non-specific myocardial damage, one was unchanged six months later, and the other was within normal limits eight years later. One showed questionable myocardial damage, but was never repeated. Another showed myocardial damage and right bundle branch block. This patient later died and was found to have a tuberculous lesion in the myocardium. Another showed right ventricular strain in 1945, but was within normal limits in 1946. The remainder showed various aberrations in the classifications already mentioned, fluctuating between abnormal and normal.

Other laboratory determinations, including alkaline phosphatase, blood calcium and phosphorus, and plasma cholesterol were made on occasional patients. However, these studies were done so irregularly that no conclusions can be drawn from them.

*Discussion*

In reviewing the literature on sarcoidosis, one is always impressed with the variation in concepts and reported material. This report may clarify some of the reasons why such variations occur.

Most of the 40 patients presented generalized symptoms of systemic infection, pulmonary lesions, or reticulo-endothelial system involvement. These facts were mirrored in the initial clinical diagnoses, the predominating symptoms, and the roentgenographic diagnosis. As far as this group of patients was concerned, diagnosis of sarcoidosis on a basis of physical findings should have been suspected readily. In a large number of cases, careful inspection, palpation, percussion, and auscultation reveal the diagnosis to the alert and trained clinician.

Within general limits, our laboratory findings are comparable to those reported in the literature. It must be emphasized again that tissue biopsy is the single most important test in confirming the diagnosis of sarcoidosis. But it is important to keep in mind

that the biopsy is of value only if it is correlated with the clinical findings.

This study records the diagnostic experience with sarcoidosis of a group of clinicians in various specialities in teaching hospitals. The course of the disease, treatment, and prognosis have not been reviewed in this report since the diagnostic problems were the primary consideration of the authors. It is believed that the results recorded are similar to those experienced in other comparable hospitals where interest and knowledge regarding sarcoidosis is equally varied. It is obvious that clinicians working in diverse specialties will approach the evaluation and diagnosis of this disease with an armementarium peculiar to their specialty. When an overall diagnostic plan is lacking, then, as observed in this report, patients are not studied completely. A patient with uveitis, for example, may not have a careful examination for evidence of systemic disease, or a patient with pulmonary lesions may not have adequate sputum studies. Again, although it is realized that the etiology is still unknown, biopsy specimens are sent routinely for histological but not for bacteriologic or mycologic examination.

It would appear reasonable to establish a plan of study for all patients with a systemic disease of chronic nature, including those suspected of sarcoidosis. This plan should include the coordinated activities of all available clinical and laboratory facilities, and the complete physical examination of these patients, together with special studies as indicated. Of particular importance would be careful studies of biopsied material or secretions for bacteria, fungi, and unusual organisms.

It is felt that if an overall plan of study were carried out, the resulting information would aid in clarifying the nature of sarcoidosis. Judging from our cases, we believe that sarcoidosis is not necessarily a disease of a single etiology, but, may be simply a systemic reaction to one or more of a variety of etiological agents or factors. Certainly, the suggested complete studies would throw light not only on sarcoidosis but also upon a large group of granulomatous and systemic diseases which await clarification.

## SUMMARY

Sarcoidosis is a chronic systemic granulomatous disease of unknown etiology which usually presents clinical findings so mild that these appear unrelated to the widely disseminated lesions which may be found on physical and laboratory examination. A representative group of cases is reviewed with emphasis placed on the problems encountered in diagnosis. The need is demonstrated for an overall plan of study to clarify the basic understanding of this disease process.

## RESUMEN

La sarcoidosis es una enfermedad crónica, sistematizada, granulomatosa de etiología desconocida con hallazgos clínicos tan moderados que no parecen en relación con las lesiones ampliamente diseminadas que pueden encontrarse al examen físico y en el examen de laboratorio. Un grupo representativo de casos se revisa recalcando los problemas que se encuentran en el diagnóstico. Se demuestra la necesidad de un plan general de estudio para aclarar el fondo de este proceso patológico.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# Treatment of Tuberculous Meningitis with Streptomycin

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## I. *Introduction*

The advent of streptomycin therapy has prolonged life in many cases of tuberculous meningitis, and on occasions, apparent cures have been noted. Thus, to cite just a single example, of 14 cases referred to by one of us in a previous publication,[1] and observed in the pre-streptomycin era from 1934 to 1938, the mortality rate was 100 per cent and the survival period ranged from 5 to 17 days after the clinical onset of the meningitis. By contrast, 10 cases were treated with the antibiotic in this hospital in the two and one-half year period between January 1947, and July 1, 1949. The status of the patients as of January 1, 1950 showed that 9 had lived from 15 to 484 days (average 148) before death intervened, while one patient was still alive 1,005 days or 33.5 months after the onset of treatment. It is obvious, however, that the results still leave much to be desired. Fundamental and provocative and still unanswered therapeutic problems confront us.

Our purpose in this paper is two-fold: (1) to record our experiences in assaying the effects of the intrathecal use of streptomycin per se; (2) to review our treated cases of meningitis in an attempt to define a plan of therapy and criteria for "cure."

## II. *The Effects of the Intrathecal Administration of Streptomycin in Non-Meningitic Patients*

To what extent does the intrathecal use of streptomycin contribute to the additional development of abnormal symptoms and signs in cases of tuberculous meningitis? This becomes of importance, particularly, in the evaluation of the spinal fluid findings in any given patient receiving such therapy. In an attempt to obtain some clarification on this point, the following control experiment was undertaken. Four patients seriously ill with far advanced pulmonary tuberculosis, but *without* meningitis, were given streptomycin intraspinally. Observations were made on specimens of the spinal fluid on each occasion *prior* to the instillation of the drug, which was diluted in 10 cc. of isotonic saline and given

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TABLE A

Effect of Intrathecal Streptomycin in Tuberculous Patient Without Meningitis

Case A: White Male, Age 67

| DATE | 9-13-48 | 9-15 | 9-17 | 9-20 | 9-22 | 9-24 | 10-1 | 10-8 | 10-15 | 11-15 | 12-17 | 12-20 | 12-22 | 12-29 | 1-10-49 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **SPINAL FLUID:** | | | | | | | | | | | | | | | |
| Color | Clear | | No Change | | - | - | - | - | - | - | - | - | - | - | - |
| Pressure (cms.) | 7.6 | 22.4 | 20.2 | 9.6 | | 10 | 10 | 30 | 20 | 13 | | | | | 6 |
| Cells | 10 | 207 | 170 | Web | 7 | 38 | 27 | | 20 | 0 | 10 | 23 | 100 | 50 | 1 |
| Protein mgm.% | 41 | 164 | 106 | 120 | 22 | 77 | 90 | 98 | 86.4 | 31.7 | 56 | 63.5 | 83 | 90 | 60 |
| Sugar mgm.% | 75 | 42 | 48 | 50 | 87 | 66 | 55 | 54.5 | 52.6 | 66.6 | 66 | 45.4 | 45.4 | 52.6 | 71.4 |
| Chlorides mgm.% | 714 | 667 | 644 | 679 | 725 | 714 | 675 | 677 | 689 | 624 | 700 | 650 | 683 | 677 | 714 |
| **STREPTOMYCIN:** | | | | | | | | | | | | | | | |
| Dosage, gms. | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | | None Given | | | 0.1 | | None Given | | |
| **FEVER:** | Temp. 103.4°—6 hrs. after first injection with return to 100° after 6 days. | | | | | | | 98.6° - 100° | | | | Temp. 102.6° 8 hrs. later and return to normal on December 21, 1948. | | | |
| **OTHER SYMPTOMS AND SIGNS:** | Nuchal rigidity, headache, mental confusion 6 hrs. after first injection and disappearance in 4 days. | | | | | | | None | | | | Headache, disorientation 8 hrs. later and disappearance on Dec. 23, 1948. | | | |

TABLE B

Effect of Intrathecal Streptomycin in Tuberculous Patient Without Meningitis

Case B: White Male, Age 27

| | DATE 9-27-48 | 9-29 | 10-1 | 10-4 | 10-6 | 10-8 | 10-15 | 11-15 |
|---|---|---|---|---|---|---|---|---|
| **SPINAL FLUID:** | | | | | | | | |
| Color | Clear | No Change - - - - - - - - - - - - | | | | | | |
| Pressure (cms.) | 3.4 | 6.6 | 3.8 | 10 | 6 | 6 | 8 | 9 |
| Cells | 0 | 0 | 0 | 0 | 0 | 0 | 8 | 0 |
| Protein mgm.% | 54 | 36.4 | 27 | 31.7 | 30 | 30 | 32.8 | 41.5 |
| Sugar mgm.% | 65 | 61 | 66.6 | 66.6 | 58.8 | 55.5 | 55.5 | 66.6 |
| Chlorides mgm.% | 720 | 714 | 754 | 727 | Q.N.S. | 709 | 712 | Q.N.S. |
| **STREPTOMYCIN:** Dosage, gms. | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | None Given | |
| **FEVER:** | Highest temperature was 100.6° on October 7, 1948. Temperature most often below 100°. | | | | | | | |
| **OTHER SYMPTOMS AND SIGNS:** | None - - - - - - - - - - - - - - - | | | | | | | |

TABLE C

Effect of Intrathecal Streptomycin in Tuberculous Patient Without Meningitis

Case C: White Male, Age 64

| | DATE 11-17-48 | 11-19 | 11-22 | 11-24 | 11-26 | 11-29 | 12-6 |
|---|---|---|---|---|---|---|---|
| SPINAL FLUID: | | | | | | | |
| Color | Clear | No Change - - - - - - - - - | | | | | |
| Pressure (cms.) | 13.2 | 18 | 18 | 16 | 14 | 9 | 12.5 |
| Cells | 0 | 0 | 120 | 110 | 25 | 50 | 110 |
| Protein mgm.% | 38.5 | 32 | 54 | 60 | 38.5 | 60 | 83 |
| Sugar mgm.% | 71.4 | 67 | 50 | 55.5 | 66.6 | 62.5 | 66.6 |
| Chlorides mgm.% | 712 | 601 | 577 | 675 | 654 | Q.N.S. | 677 |
| STREPTOMYCIN: Dosage, gms. | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | None |
| FEVER: | Highest temperature 100.4 on Nov. 18, 1948. Otherwise, temperature below 100°. | | | | | | |
| OTHER SYMPTOMS AND SIGNS: | None - - - - - - - - - - - - - - | | | | | | |

TABLE D

Effect of Intrathecal Streptomycin in Tuberculous Patient Without Meningitis

Case D: White Male, Age 46

| | DATE 12-11-48 | 12-13 | 12-15 | 12-20 | 12-22 | 12-24 | 12-31 | 1-10-49 |
|---|---|---|---|---|---|---|---|---|
| SPINAL FLUID: | | | | | | | | |
| Color | Clear | No Change - - - - - - - - - - - - | | | | | | |
| Pressure (cms.) | 4 | 12 | 9 | 11 | | | | 9.8 |
| Cells | 5 | 1000 | 40 | 30 | 530 | 60 | 10 | 2 |
| Protein mgm.% | 40 | 108 | 90 | 51.4 | 44.5 | 47.6 | 56.7 | 51.4 |
| Sugar mgm.% | 58 | 45 | 46 | 55.5 | 58.8 | 63.5 | 62.5 | 80 |
| Chlorides mgm.% | 725 | 714 | 714 | 672 | 694 | 680 | 724 | 702 |
| STREPTOMYCIN: | | | | | | | | |
| Dosage, gms. | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | None | None |
| FEVER: | Temperature rose to 101° on Dec. 12, 1948, then dropped to normal; and up to 101.8° on Dec. 15, 1948 and below 100° thereafter. | | | | | | | |
| OTHER SYMPTOMS AND SIGNS: | None - - - - - - - - - - - - - - | | | | | | | |

slowly after at least an equal amount of fluid had been removed. The dosage of the antibiotic per injection was about the same that we have come to use now therapeutically for meningitis. The fluid was examined also during rest periods when no streptomycin was injected. The detailed laboratory findings and the reactions encountered are presented in Tables A, B, C, D. In summary, the following are the significant observations:

(a) Only one, (Case A), of the four patients exhibited abnormal symptoms and signs, as manifested by fever, nuchal rigidity, headache and disorientation; these disappeared after several days.

(b) In three patients, (Cases A, C, D), who received injections of 0.1 gram, abnormal spinal fluid findings were found in variable degree, 48 hours after the first injection. The color remained clear throughout, but the pressure was elevated at times, and the cell count increased. After two or three injections, the predominant type of cell shifted from the polymorphonuclear leukocyte to the lymphocyte. As regards the chemistry of the fluid, elevation of the protein fraction was noted early and persisted longest; the chlorides were frequently depressed, but the sugar remained essentially within normal limits. The duration of these abnormalities ranged from 2.5 to 6 weeks (Cases A and D). In Case C, an adequate number of post-streptomycin spinal taps could not be done. Case B, who received six injections of 0.05 gram of streptomycin showed no unusual changes in the fluid.

Within the limits of this experiment, broad and final conclusions are unwarranted. The impression, nevertheless, remains that streptomycin in the dosage of 0.1 gram intrathecally has an irritative and variable effect on the meninges and that it would probably be difficult to determine, in any specific case of tuberculous meningitis, what fraction of the abnormal spinal fluid changes could be ascribed to this dosage of streptomycin, and what to the disease process itself. However, one might expect the changes in the fluid due to the super-imposed chemical meningitis to disappear after several weeks. Perhaps persistence of these findings (particularly increased cell count and protein), beyond a period of six weeks after cessation of streptomycin, should be attributed to the tuberculous involvement and not to the antibiotic.

### III. *Summary of Treated Cases of Tuberculous Meningitis and Results*

Of the 10 patients, two were colored and eight white; nine were young adults and one a child. It is generally agreed that when the meningitis is part and parcel of a generalized hematogenous tuberculosis, the prognosis is less favorable. Hinshaw[2] reported four casese associated with miliary tuberculosis and all died. In

TABLE E

Cases of Tuberculous Meningitis

| | Case | Age, Sex, Race | Duration of Tuberc. | With Acute Miliary Tuberc. | Duration (Days) of Meningeal Symptoms Prior to Rx |
|---|---|---|---|---|---|
| GROUP A: | | | | | |
| (1) | G.M. | 32 F W | 7 yrs. | No | 8 |
| (2) | A.D. | 35 M W | 1 yr. | No | 7 |
| (3) | W.B. | 33 M W | 2 yrs. | No | 15 |
| (4) | A.W. | 27 F W | 5 yrs. | Yes | 4 |
| (5) | A.J. | 3½ F W | Calcified 1° Inf. | No | 4 |
| GROUP B: | | | | | |
| (6) | G.B. | 39 F W | 1 yr. | No | 2 |
| (7) | C.C. | 37 M W | 2 yrs. | No | Abnormal neurological symptoms for about 5 mos. and meningitis about 10 days. |
| (8) | J.C. | 34 M C | 2 yrs. | No | 2 |
| (9) | M.G. | 30 M C | 6 yrs. | No | 4 |
| (10) | H.H. | 28 M W | 6 mos. | Yes | 10 |

TABLE F

Therapy and Results with Streptomycin

| | Case | Route | Dose Grams | Interval | RX. Days | Total Dose, Grams | Reactions | Survival Time From Onset of RX. |
|---|---|---|---|---|---|---|---|---|
| GROUP A: | | | | | | | | |
| (1) | G.M. | I.M. | 2 | Q.D. | 30 | 60 | Pain in legs, thighs with ITH. inj. | 97 days or 3.25 mos. Died. |
| | | ITH. | 0.25 to 0.5 | 17 injections in 30 days | | 7.5 | | |
| (2) | A.D. | I.M. | 1.0 to 2.0 | Q.D. | 152 | 240 | As above, plus headache, vomiting. | 252 days or 8.4 mos. Died. |
| | | ITH. | 0.125 to 0.5 | 63 injections in 77 days | | 31+ | | |
| (3) | W.B. | I.M. | 1.0 | Q.D. | 92 | 92 | Headache, vertigo. | 484 days or 16 mos. Died. |
| | | ITH. | 0.125 to 0.10 | 25 injections in 30 days | | 3+ | | |
| (4) | A.W. | I.M. | 1.0 to 2.0 | Q.D. | 94 | 165 | Same as G.M. also nuchal rigidity. | 97 days or 3.25 mos. Died. |
| | | ITH. | 0.125 to 0.25 | 36 injections in 51 days | | 5+ | | |
| (5) | A.J. | I.M. | 1.0 to 2.0 | Q.D. | 90 | 116 | Unsteady gait. | 1,005 days or 33.5 mos. Living. |
| | | ITH. | 0.04 to 0.10 | 16 injections in 28 days | | 1.5 | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| GROUP B: | | | | | | | | |
| (6) | G.B. | I.M. | 1.0 | Q.D. | 25 | 25 | None. | 24 days. Died. |
| | | ITH. | 0.1 | 17 injections in 17 days | | 1.7 | | |
| (7) | C.C. | I.M. | 1.0 | Q.D. | 15 | 15 | None. | 15 days. Died. |
| | | ITH. | 0.1 | 5 injections in 5 days | | 0.5 | | |
| (8) | J.C. | I.M. | 1.0 | Q.D. | 25 | 25 | None. | 33 days. Died. |
| | | ITH. | 0.05 | 24 injections in 24 days | | 0.6 | | |
| (9) | M.G. | I.M. | 1.0 | Q.D. | 120 | 120 | Partial deafness (left). | 275 days or 9.2 mos. Died. |
| | | ITH. | 0.05 to 0.10 | 26 injections in 120 days | | 2.1 | | |
| (10) | H.H. | I.M. | 1.0 | Q.D. | 47 | 47 | None. | 57 days. Died. |
| | | ITH. | 0.1 | 21 injections in 46 days | | 2.1 | | |

TABLE G
Findings in Autopsied Cases

| | Case | Gross Findings | Histological Findings—C.N.S. |
|---|---|---|---|
| (1) | G.M. | (a) Diffuse lymphatic Tuberc. of nodes with large retroperitoneal mass of glands. (b) Nodular Tuberc. with minimal hematog. lesions in both lungs (3) Tubercles in liver and kidney (4) Focal Tuberc. colitis (5) Tuberc. meningitis of all aspects of brain and cerebellum; also tuberculoma of septum bet. right and left ventricles. | Extensive caseous Tuberc. process involving the vessels, pia arachnoid and much of brain substance. Many large vessels showed endarteritis. No evidence of healing. |
| (3) | W.B. | (a) Lungs—old nodular foci, minimal hematog. dissemination, left pleural effusion; (b) Brain—thin caseous exudate and congestion of pial vessels; serial sections of cerebrum and cerebellum showed no grossly visible tubercles. | No significant changes in cerebral lobes. Sections through cerebellum, pons, spinal cord showed foci of perivascular round cell infiltration with scattered small areas of necrosis and occasional giant cells. |
| (7) | C.C. | Past history of tuberc. of left hip; also left nephrectomy (Tuberc.). Autopsy showed (a) bilat. pulm. Tuberc. with tubercles in lungs, liver, spleen; (b) bilat. psoas abscess with Tuberc. of lumbar vertebrae; (c) Brain—multiple miliary and nodular tubercles of cerebrum and cerebellum with Tuberc. of meninges at base. | Multiple sections through cerebrum showed isolated large caseous areas surrounded by zone of inflammation. Extensive Tuberc. of meninges from base of brain near cerebellum. Wide zones of caseation necrosis about blood vessels. |
| (9) | M.G. | (a) Lungs—fibrocavernous Tuberc. L.U.L. with bronchogenic spread; left empyema; (b) Tuberc. of seminal vesicles, prostate and epididymi with atrophy of left testicle and Tuberc. of right testicle; (c) Brain—chr. Tuberc. meningitis involving primarily base of brain with dilatation of lateral and third ventricle. | Cerebrum—diffuse inflammation of pia arachnoid with monocytes, lymphocytes and occasional "polys"; typical tubercles not seen. Cerebellum—similar inflammation with tubercles in pia arachnoid; vessels extensively involved. Third Ventricle and Cerebral Peduncles—marked dilatation of vessels with areas of focal caseation necrosis. |

the series of McDermott et al,[3] the seven out of nine patients with tuberculous meningitis complicating miliary spread also died. Bunn[4] reviewed 100 cases of miliary and meningeal tuberculosis treated with streptomycin; 25 of these had both conditions at the onset of therapy and 20 died (80 per cent); five remained alive for an average of 7.4 months after treatment was started. Of 43 cases of tuberculous meningitis without acute miliary tuberculosis, 27 died (62.7 per cent) and those that lived had a survival of four to 14 months after institution of therapy. Two patients in our group (Cases 4 and 10) had an associated acute dissemination of tuberculosis, although four others at one time or another revealed clinical evidence of hematogenous extrapulmonary foci.

A factor which on general principles must be considered as one of prognostic significance is the duration of meningitis prior to the institution of therapy with streptomycin. However, it must be admitted that in this small group of cases, there appeared no consistent direct relationship between this factor and length of survival.

Tables E and F summarize the pertinent clinical and therapeutic aspects in each case. Necropsies were done in four cases and these findings are mentioned briefly in Table G. Significant pathological evidence of healing of the meningitis was not observed.

While the combined intramuscular and intrathecal routes of administration of streptomycin have been widely accepted as fundamental in the therapy of tuberculous meningitis, one of the chief problems has been the dosage to be employed and the length of treatment. It so happened that the first five cases (Group A) in this report developed meningitis during the first four months of 1947 when the therapeutic regimen with streptomycin was more empirical than at present. The parenteral dosage of the drug in this group ranged from 1.0 to 2.0 grams daily and was given for at least three months in all but one patient (Case 1). The intrathecal dosage used on several occasions was definitely excessive according to current standards and resulted in the development of toxic and irritative symptoms which improved or disappeared entirely after the dosage was reduced. No constant pattern was followed as to the frequency of these injections. Yet the survival period (dated from the onset of therapy to death) in this earlier Group A was definitely longer and varied from 97 to 484 days with an average of 233 days or almost eight months. Case 5, alive now for 33.5 months, merits some comment. This child was discharged on August 6, 1947 with the tuberculous meningitis (tubercle bacilli had originally been recovered from the spinal fluid) arrested, and with symptoms of a mild residual speech defect and a slightly unsteady gait (the latter symptom being attributed to strepto-

mycin). She was re-admitted on January 12, 1948 with recurrent symptoms and signs of meningitis but the spinal fluid was purulent and meningococci were present. Treatment was promptly instituted with salfadiazine and penicillin and because of the previous tuberculous inflammation, streptomycin therapy was also resumed. The patient made an uneventful recovery, was discharged on February 27, 1948 and has remained well since, without any neurological sequelae.

In the second group of five cases (Group B), the intramuscular dose of streptomycin was uniformly 1.0 gram daily and the maximum intrathecal dose 0.1 gram. The life span varied from 15 to 275 days with an average of 81 days or 2.7 months. Two patients (Cases 8 and 10) received supplementary antibiotic therapy, promizole and para-aminosalicylic acid in the former and PAS alone in the latter. In both instances this therapy was of very short duration (less than one month) and of no significance. One patient (Case 9) developed partial deafness which was considered as a toxic drug reaction.

In summarizing the final results, it is noted as mentioned earlier, that the mortality rate was 90 per cent and one patient (10 per cent) was alive and well 33.5 months from the onset of treatment. Incidentally, considerable regression of the miliary foci was noted on the x-ray films of the chest in the two patients with acute hematogenous dissemination.

## IV. *Comment*

The diagnosis of tuberculous meningitis is not difficult. The neurologic symptoms and signs are generic for meningitis and not pathognomonic but when they occur in a patient with known tuberculosis, the diagnostic probability is increased. However, examination of the cerebrospinal fluid is of paramount importance. While the presence of the tubercle bacillus makes the diagnosis unequivocal, active therapy should, of course, be started before it is recovered. In seven of our 10 cases, the cultures or animal innoculation tests were positive. Of the remaining three cases, the diagnosis was confirmed by necropsy in two (Cases 7 and 9) while the other (Case 10) had the classical clinical picture of associated miliary tuberculosis. Although predominance of lymphocytes is the rule, two patients showed 90 and 100 per cent polymorphonuclear leukocytes on the initial cell counts. It is important to recall that the early cellular response in tuberculous serous membrane involvement may be of this latter type.

Routine study of the fluid also revealed that the sugar was subnormal in nine cases, the protein elevated in a similar number and the chlorides depressed in seven. All of the results mentioned

above referred to the findings prior to the institution of therapy with streptomycin.

In interpreting the significance of the C.S.F. findings after treatment has been begun, several things deserve attention: (1) the probable superimposed chemical meningitis produced by streptomycin which may persist for several weeks and which has already been alluded to; (2) as the meningitis improves, the sugar tends to return toward normal before the protein and chlorides. Lincoln and Kirmse[5] also state that the Levinson test is positive and the colloidal gold curve is abnormal in the active phase of the disease but return to normal as the process comes under control; (3) furthermore, conversion to normal as far as the cytology and chemistry of the C.S.F. are concerned is more significant prognostically than conversion to a negative culture for tubercle bacilli. This was best demonstrated in the case of W.B., a white male, 33 years of age, in whom the first spinal fluid was positive for tubercle bacilli on guinea pig injection. Beginning April 22, 1947 he received 1.0 gram of streptomycin intramuscularly for 92 days and streptomycin intrathecally in the dose of 0.125 to 0.10 gram for 25 doses during a span of 30 days. All symptoms and physical signs of meningitis disappeared in July, 1947. This status persisted and he was discharged in June, 1948. The patient was seen on several occasions thereafter and felt well until August 24, 1948 when he became febrile and irrational. He was re-admitted two days later in a semi-comatose state and died within 12 hours. In retrospect, his status was evaluated erroneously. Too much importance was attached to the patient's apparent well being for over a year. Too much reliance was placed on the 25 consecutive negative culture reports for tubercle bacilli in the spinal fluid examinations done during and after cessation of therapy. The increased cell counts and the abnormal chemistry in these studies were attributed to effects caused by streptomycin. Actually, they reflected low grade chronicity of the infection which exascebated itself with sudden explosiveness. The spinal fluid on re-admission revealed 460 cells, 180 mgm. per cent protein, 12 mgm. per cent sugar, 527 mgm. per cent chlorides and this specimen was subsequently found to be positive on culture for tubercle bacilli. (See Table G for postmortem findings). There were six other patients who showed temporary clinical remissions and conversion of the bacillary cultures, with a similar discrepancy in the cytological and chemical features of the spinal fluid.

Early in meningitis, there is hypervascularization and increased permeability of the meninges. Later on the exudate increases and in the chronic stage, fibrous organization and tuberculous arteritis occur and the vascularity diminishes. This fact emphasizes the

urgency for diagnosis in the early stage and the prompt use of antibiotic therapy to obtain maximum access to the tuberculous foci and to minimize damage to the brain. However, in published reports there is no conformity as to what comprises adequate treatment or when it should be stopped or what constitutes arrest of the disease. There is also considerable discrepancy in the results of treatment. Bunn[6] stated that the mortality in children has been reported as ranging between 15 to 66 per cent and in adults from 50 to 90 per cent (the minimum post therapy observation period was five months). Those cases in particular which have a relatively long remission and then relapse should furnish good material for possible improvement in the efficacy of treatment.

In reviewing our experiences and those of others, the following approach to the therapy of tuberculosis meningitis may be productive of more favorable results. It is intended as a flexible and not a rigid formulation which should be adapted to the individual patient. Intensive treatment by the combined intramuscular and intrathecal routes is the basic cornerstone. Marshall et al.,[7] in reporting on 105 proved cases, mentioned that of the patients who received streptomycin parenterally only, 11 per cent made good progress compared with 35 per cent in the group which was given the drug simultaneously by both routes. It is also generally accepted that the administration of streptomycin by intracisternal or intraventricular injection is potentially more dangerous and rarely necessary.

Realizing the importance of making an early diagnosis, therapy is promptly instituted:

(1) Dihydrostreptomycin — is given intramuscularly usually in the dosage of 2 to 3 grams daily in adults and 1.0 gram in children; duration of therapy, 120 to 180 days, preferably the latter.

(2) Streptomycin intrathecally — although improvement in the preparation of the dihydro product will probably make possible its use by this route also—may be administered in the dosage of 0.1 gram daily for four weeks, then every other day for two weeks and twice weekly for an additional two weeks. By this attack, an early and sustained antibiotic "barrage" is probably achieved. The appearance of toxic manifestations will require reduction in the dosage (0.05 gram). Intrathecal therapy requires the use of an isotonic solution of streptomycin which should be given very slowly in 10 cc. of the diluent. The necessary determinations should be made, as discussed earlier, on the removed specimens of spinal fluid. Moreover, diagnostic lumbar taps should be done (post therapy) at least monthly for 12 months with especial reference to the cell count and the constituents of protein, sugar and chlorides as indices for activity of the infection (allowing for the factor

of chemical irritation by the streptomycin). If the spinal fluid studies indicate an exascebation or if clinical relapse becomes evident, another course of streptomycin should be resumed. In order to minimize injury to the brain by the deposits of fibrin, and retard the formation of connective tissue which may produce spinal block, heparin or streptokinase[8] are now being advocated as intrathecal adjuvants to streptomycin.

(3) Supplementary antibiotic therapy is also indicated in view of the seriousness of tuberculous meningitis. To delay the emergence of streptomycin resistant tubercle bacilli, para-aminosalicylic acid (9 to 12 grams daily by mouth) is warranted. Lincoln et al,[5,9] who have made significant contributions to the therapy of tuberculous meningitis in children advocate the use of promizole (usual dose 1 to 5 grams daily orally) which they believe enhances the effect of streptomycin. These drugs should be given concurrently with streptomycin, although continued use of promizole for many months afterward has also been recommended.

(4) As with any grave disease, the patient must be regarded as a whole. Particular attention should be directed to maintain an adequate nutritional state. A dietary high in calories, protein and vitamins should be started as early as possible. If the patient is unable to take oral nourishment, no time should be lost in administering parenterally, electrolytes, vitamins and protein hydrolysates. Transfusions may also be necessary.

Can we define an apparent "cure" in tuberculous meningitis? We would be willing to utilize these criteria:

(1) Normal cerebrospinal fluid, cytologically, chemically and bacteriologically as observed in a minimum of 12 consecutive diagnostic lumbar taps over a 12 month period following the cessation of therapy.

(2) The patient should have no symptoms or physical signs referable to a diagnosis of tuberculous meningitis during this same length of time.

## SUMMARY

1) The results of an experiment to determine the effects of intrathecally administered streptomycin in a small group of non-meningitic patients are recorded.

2) Particular emphasis is placed on the evaluation of cerebrospinal fluid findings during and after cessation of therapy.

3) A group of 10 cases of tuberculous meningitis treated with streptomycin is reported in which one patient (10 per cent) was still alive and well 33.5 months after onset of therapy.

4) Some important factors which influence length of survival are:

(a) duration of meningitis prior to onset of therapy.

(b) presence or absence of associated intracranial tubercles or tuberculomata.

(c) presence or absence of associated acute generalized miliary tuberculosis.

(d) age of patient (child or adult).

(e) adequacy of treatment.

5) A plan of treatment is outlined and criteria for an apparent "cure" are suggested.

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Appreciation is expressed to Dr. B. P. Potter, Chief of Medical Division I for consent to include the 4 cases of meningitis from his Service in this report.

## RESUMEN

1) Se refieren los resultados de un experimento para determinar los efectos de la estreptomicina intrarraquídea en un pequeño grupo de enfermos sin meningitis.

2) Se recalca la importancia de los hallazgos en el líquido céfalo-raquídeo durante y después del tratamiento.

3) Se presenta un grupo de 10 casos de meningitis tuberculosa tratados con estreptomicina de los que uno aún vive en buenas condiciones, 33.5 meses después del principio del tratamiento.

4) Algunos factores importantes que influyen en la duración de la sobrevida son:

(a) Duración de la meningitis antes del principio del tratamiento.

(b) Presencia o ausencia de tubérculos intracraneales o de tuberculomas.

(c) Presencia de tuberculosis aguda miliar asociada.

(d) Edad del enfermo (niño o adulto).

(e) Tratamiento adecuado.

5) Un plan de tratamiento o el criterio para obtener una "curación" aparente se sugieren.

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# Artificial Pneumoperitoneum in the Treatment of Pulmonary Emphysema*

## A Preliminary Report

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The treatment of pulmonary emphysema with artificial pneumoperitoneum was first introduced by Reich[1] in 1924. A subsequent report of Piaggo Blanco[2] and his associates in 1937 indicated that this form of therapy provided definite benefit in a significant number of cases. Nevertheless, artificial pneumoperitoneum has not been widely employed in the treatment of pulmonary emphysema.

The purpose of this report is to review briefly the pneumodynamics of pulmonary emphysema, to consider the physiological basis for treating emphysema with artificial pneumoperitoneum, and to present a preliminary report of the therapeutic results obtained in seven severe cases.

In pulmonary emphysema the lungs are in a state of overdistention, with enlargement and fusion of air sacs and reduction in the number of alveoli due to atrophy of inter-alveolar septa. This results in a reduction in the total respiratory surface. There is also reduction in pulmonary elastic tissue. The lungs, when removed from the thorax, do not collapse normally, but remain in an over-distended state. In addition, there is thickening of the alveolar and capillary walls and a general increase in interstitial tissue. Capillaries may become occluded. As a result of dorsal kyphosis and a more horizontal position of the ribs, the antero-posterior diameter of the bony thorax increases, producing a barrel-shape chest. The position of the chest eventually becomes one of almost full inspiration. The level of the diaphragm is much lower than normal and its excursion may be limited. Indeed, it may become fixed and not move at all or, worse still, it may exhibit paradoxical movement. Respiration therefore becomes mainly costal.

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As a result of these changes, expiration no longer remains a passive movement, but requires forcible contractions of the expiratory muscles. The residual air is greatly increased and may be two or three times normal. The tidal air is normal or slightly reduced, but the vital capacity is lowered by as much as 20 to 60 per cent. When the patient is asked to inspire deeply he is unable to expel all the air during the next expiration, even though expiration is forced. A series of expirations must occur before the chest returns to its original size. Visual proof of this fact is provided when a patient, following maximal inspiratory effort, is unable to blow out a candle. The total lung volume remains normal or may be increased (Figure 1).

The primary biochemical changes associated with severe pulmonary emphysema are essentially those of carbon dioxide retention and anoxemia. These abnormalities are the direct result of impaired gaseous exchange. Wilson[6] studied the effect of hyperventilation in patients with cardiac dyspnea, and in a group of patients with chronic pulmonary emphysema. In the emphysema group the initial carbon dioxide tension of the blood was elevated and oxygen saturation diminished. The blood pH was normal as a result of a compensatory increase in plasma bicarbonate. While the values before and after hyperventilation in normal subjects and in patients with cardiac dyspnea were similar, voluntary hyperventilation did not alter appreciably the initial values in

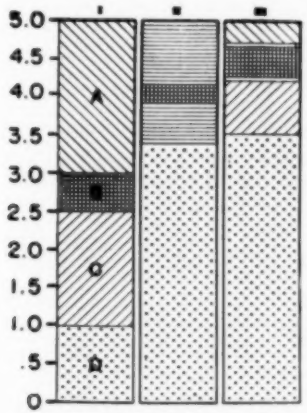


FIGURE 1: Diagram showing subdivisions of lung air (in liters). I normal, II asthma and III emphysema. A, complemental air; B, tidal air; C, supplemental or reserve air; D, residual air. The horizontal lines in II and III indicate the relative extent of respiratory movement. (Modified from Best and Taylor, The Physiological Basis of Medical Practice, Fourth Edition, The Williams and Wilkins Company, Baltimore).

the emphysema group. It is to be recalled that in emphysema the respiratory center is relatively insensitive to carbon dioxide. It is obvious that these patients are particularly vulnerable to metabolic and respiratory acidosis.

Prinzmetal and Kountz[5,7] have attributed limitation of diaphragm movement to the fact that in emphysema the intrapleural and intra-abdominal pressures approach one another. On the basis of their studies they recommended the use of an especially constructed abdominal belt. Measurements of intrapleural pressure were made before and after the application of the belt. In each instance the intrapleural pressure, characteristically close to atmospheric pressure in emphysema, become more negative after application of the belt. Independently of these investigators, the use of an abdominal binder was also advocated by Christie[8] and Gordon.[9] Banyai[10] has pointed out that greater elevation of the diaphragm may be obtained by sustained pneumoperitoneum than by abdominal support.

Pneumoperitoneum thus offers a direct and simple means of producing a more physiological diaphragm function by (1) elevating the diaphragm without offering undue resistance to downward (inspiratory) movement, and (2) increasing intra-abdominal pressure, allowing for the development of a more negative intrapleural pressure during inspiration, and a more rapid return of the diaphragm to an elevated resting position during expiration. The use of the voluntary muscles of the abdominal wall as a respiratory adjunctive is also rendered more effective by pneumoperitoneum.

## *Material and Methods*

Seven patients were studied objectively before and after treatment with vital capacity measurements, chest roentgenograms in maximal inspiratory and expiratory positions and exercise tolerance tests, utilizing a Master 2-step and a Millikan oximeter to measure change in arterial oxygen saturation. Because the emphysematous patient on prolonged expiratory effort may display an almost normal vital capacity, a stop-watch was used to limit the expiratory effort to precisely three seconds, in order to measure more accurately the degree of true functional respiratory impairment. This is referred to hereafter as the three second vital capacity. The mean of at least three readings was used, and in the majority of cases, the results of more than one observer were compiled. The number of trips over the Master 2-step that each patient was asked to make was determined by preliminary trial, and in each instance the number of trips required represented only slightly less than the maximal effort possible on the part of

the patient. Relative changes in arterial oxygen saturation during the exercise were measured by the Millikan Oximeter and recorded by means of an Esterline-Angus constant recording galvonometer connected to the Oximeter.

The initial pneumoperitoneum varied between 400 and 1200 cc. of air. The second and third injections were given at intervals of three or four days, and the volume of air injected was increased to 800 to 1600 cubic centimeters. A closing pressure of eight to 12 centimeters of water has usually been maintained by the injection of 800 to 1200 cc. of air at weekly or bi-weekly intervals. There is an optimal amount for each patient, and an effort is made to determine this amount.

*Case 1 (C.G.):* A 64 year old white male had frequent upper respiratory tract infections in early childhood, followed by chronic cough. He had exertional dyspnea for more than five years prior to treatment. In 1947 he was hospitalized because of chronic fibroid pulmonary tuberculosis, at which time the blood pressure was 200/100 and he developed signs of marked cardiac insufficiency. He entered a sanitorium where he was placed on a cardiac regimen and experienced moderate improvement. Anginal pain developed which was relieved by nitroglycerin. An abdominal binder was tried but afforded little relief. Pedal edema developed in spite of continued cardiac treatment. Following initial hospitalization he was admitted several times because of aggravation of cardiac symptoms. With strict cardiac management on each admission he would show symptomatic improvement. However, he was never free of exertional dyspnea and he became virtually incapacitated. Bronchodilators and antihistaminics failed to control asthma-like symptoms. There was no polycythemia. Emphysema was severe.

On February 25, 1949 his three second vital capacity was 1100 cc. Fluoroscopically the diaphragm was flattened and moved less than one centimeter. An initial pneumoperitoneum of 400 cc. of air was given, and before the needle was withdrawn he stated that he was able to breath better. Fluoroscopy immediately following pneumoperitoneum showed a smoothly rounded diaphragm with an excursion of about 2.5 cm. During the following months he received refills twice weekly and after one month of treatment had shown striking improvement, even though bronchodilator drugs had been discontinued. He had no further angina. Since March 1949 he has received refills at weekly intervals of 800 to 1200 cc. of air. On October 1, 1949 he was readmitted because of severe and progressive epigastric pain of 12 hours duration accompanied by the passage of a bloody stool six hours prior to admission. Air was allowed to escape from the peritoneal cavity with almost complete relief of the pain. About five hours later the pain returned but was less severe. This gradually subsided and the following day, after turning over in bed, he noted a "popping" sensation and the residual pain immediately disappeared. Since then there has been no recurrence of the pain. On October 7, 1949 the pneumoperitoneum was reinstated. He has continued to receive air without difficulty, and during this time has maintained his three second vital capacity between 1600 and 2200 cc., 500 cc. or more over pretreatment values. One other factor in the management of this

case should be mentioned, namely, the distention by air of a bilateral inguinal hernia. Although this has been troublesome, management has been fairly satisfactory with a truss.

The exact nature of the attack of abdominal pain and bloody stool experienced by this patient is not clear, except for the fact that it was relieved by reducing the pressure of the pneumoperitoneum. It is our feeling that air may have been trapped beneath a section of mesentery. The sudden relief the patient experienced on turning over in bed suggests this explanation also.

The results in this case were impressive, moreover, we believe that coexisting arteriosclerotic and hypertensive heart disease limited the extent to which improvement occurred.

*Case 2 (W.B.):* A 69 year old white male had been in good health until five years prior to treatment, when he had a fairly severe attack of influenza, following which there developed severe exertional dyspnea, accompanied by a productive cough. There was marked increase in the antero-posterior diameter of the chest. There was no evidence of cardiac decompensation. Bronchograms were normal. There was no polycythemia.

Dyspnea increased to the point of complete incapacitation. It became impossible for him to stand and talk without marked discomfort. During the eight years he suffered from dyspnea and marked limitation of activity, he always obtained some relief while lying flat, especially if the feet were elevated.

In March, 1949 fluoroscopy of the chest revealed no detectable movement of the diaphragm. The three second vital capacity was 500 cc. An initial pneumoperitoneum of 1100 cc. was administered following which fluoroscopy revealed marked scalloping of the diaphragm on both sides, especially on the right, but motion had increased, especially on the left. During the following month he received injections twice weekly of between 600 and 1200 cc. of air. During the next two months he was given weekly injections of approximately 1000 cc. of air. Since that time he has had them bi-weekly.

| CASE | 3-SECOND VITAL CAPACITY | | EXERCISE TOLERANCE | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | BEFORE $R_1$ | | | AFTER $R_1$ | | |
| | BEFORE $R_1$ | AFTER $R_1$ | NUMBER MASTER 2-STEP TRIPS | TIME | PERCENT ARTERIAL $O_2$ DESATURATION | NUMBER MASTER 2-STEP TRIPS | TIME | PERCENT ARTERIAL $O_2$ DESATURATION |
| CAG | 1100cc | 1600cc | | | | | | |
| 2 WB | 600 | 1200 | 8 | 1½min | 5% | 8 | 1min | 2% |
| 3 JEP | 1200 | 3100 | 22 | 2 | 3% | 22 | 1¼ | 2% |
| 4 JBM | 1200 | 1700 | 14 | 1 | 3% | 14 | 50sec | 0 |
| 5 VHC | 1400 | 1850 | 20 | 1½ | 5% | 20 | 1½ | 3% |

TABLE I: Summarizing three second vital capacity measurements and exercise tolerance studies using the Master 2-step and the Millikan Oximeter, before and after treatment with artificial pneumoperitoneum. In each case there is a gain in vital capacity following treatment. Arterial oxygen desaturation following exercise is less after treatment in every case, although in cases three and five this difference is within the limits of error of the Oximeter used. However, in case three, the exercise was performed at a faster rate.

During the first three months of therapy there was little evidence of improvement, and the vital capacity did not increase significantly. However, after three months, improvement began and although it has not been marked, he is now able to move without the extreme dyspnea that limited him at first. After seven months of therapy the three second vital capacity had increased to 1000 cc., a gain of 500 cc. Prior to treatment he raised about a pint of mucoid sputum daily; following treatment, only two to three ounces.

Therapy in this patient appears to have been effective. Although the results have not been striking, the patient has progressed from a state of severe to one of mild incapacitation. Diaphragmatic excursion has increased to 2 cm. or more on each side. The maximum inspiratory and expiratory diaphragm positions before and after treatment are shown in figure 2. Exercise tolerance and vital capacity studies are recorded in the table.

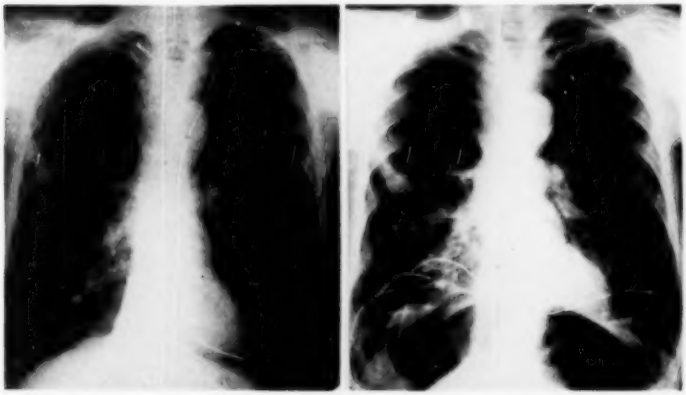

FIGURE 2, Case 2: From posteroanterior x-ray films taken before and after artificial pneumoperitoneum. These and figures 3, 4 and 5 were taken in the maximal inspiratory position. Another film was immediately obtained, in each instance, in the maximal expiratory position. The former film was then carefully superimposed on the latter, and the position of the diaphragm in maximum expiration indicated by crayon. The increased excursion made possible by pneumoperitoneum is readily apparent. The scalloped appearance of the right leaf of the diaphragm seen in the post-treatment film is thought to represent diaphragmatic crura.

*Case 3 (J.P.)*: A 68 year old white male was admitted March, 1949. He had suffered from bronchial asthma for 30 years which was not very troublesome until five years before admission when he began to have as many as five or more attacks daily. These generally responded well to epinephrine. However, six months prior to admission, the attacks became more frequent and severe, and they failed to respond well to epinephrine. Increasing amounts of intravenous aminophylline were required during this period. He developed exertional dyspnea which steadily increased in severity and frequently initiated asthmatic attacks. He became almost totally incapacitated. For two months he "practically lived" in the emergency room of the city hospital where it was common for him to receive

50 to 70 cc. of aminophylline intravenously daily. He had a chronic productive cough.

He was well developed. The blood pressure was 110 80. Asthmatic breathing was almost continuous and dyspnea occurred with the slightest movement. The shape of his chest was typical of emphysema. Percussion was hyper-resonant and sibilant rales were heard over both lung fields. The heart was not remarkable. There was no polycythemia. Fluoroscopy of the chest revealed a flattened diaphragm with little or no motion. The three second vital capacity was 1200 cc. Initial pneumoperitoneum of 600 cc. of air was given March 24th. Five days later when the third injection was made the three second vital capacity was 2200 cc., an increase of 1000 cc. He was having much less asthma and this was readily controlled with epinephrine. Fluoroscopy of the chest revealed a smoothly elevated diaphragm with good excursion bilaterally. Since March of this year he has been maintained on weekly injections of 800 to 1200 cc. of air. He has shown progressive clinical improvement and now has but slight limitation of activity because of exertional dyspnea, and no longer experiences asthmatic attacks induced by exertion. Spontaneous attacks of asthma are easily controlled by 0.2 gram of aminophylline at bedtime and infrequent injections of epinephrine. At his last visit the three second vital capacity was 3100 cc., 1900 cc. more than before the institution of pneumoperitoneum.

This patient has been almost completely rehabilitated and is now able to perform a full day's work as an elevator operator without significant respiratory distress. The maximum inspiratory and expiratory diaphragm positions before and after treatment are shown in figure 3. Exercise tolerance and vital capacity studies are indicated in the table.

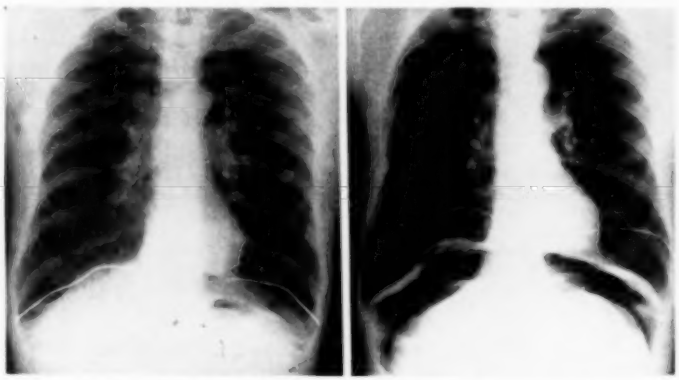

FIGURE 3. Case 3: From x-ray films showing limits of maximal diaphragm excursion before and after pneumoperitoneum treatment. For a description of technique, see legend, figure 2.

*Case 4 (J.B.M.):* A 59 year old white male was admitted because of dyspnea. He had been in good health until about two and one-half years prior to admission when he noted the onset of mild wheezing, dyspnea, orthopnea and a slightly productive cough. These symptoms progressed unfavorably until about one year prior to admission. Since that time they

have changed little. No seasonal variation was noted. The family history included asthma.

He was moderately thin and not in acute distress. The blood pressure was 140 90. The respiratory rate was slightly increased. The chest was of the typical barrel configuration. The percussion note was hyperresonant. No rales were heard. Expiration was slightly prolonged. The heart was not remarkable. The three second vital capacity was 1200 cc. He was given an initial pneumoperitoneum of 1200 cc. of air. Two days later he was given an additional 1000 cc. of air. He was then discharged from the hospital to the out-patient department where he has been given about 1000 cc. of air at bi-weekly intervals.

The three second vital capacity in this case increased from 1200 cc. to 1700 cc. following pneumoperitoneum. The patient is considerably less dyspneic, wheezes less and is extremely pleased with his result. We consider him definitely improved. The diaphragms move well. The maximum inspiratory and expiratory diaphragm positions are shown in figure 4. Exercise tolerance and vital capacity measurements are recorded in the table.

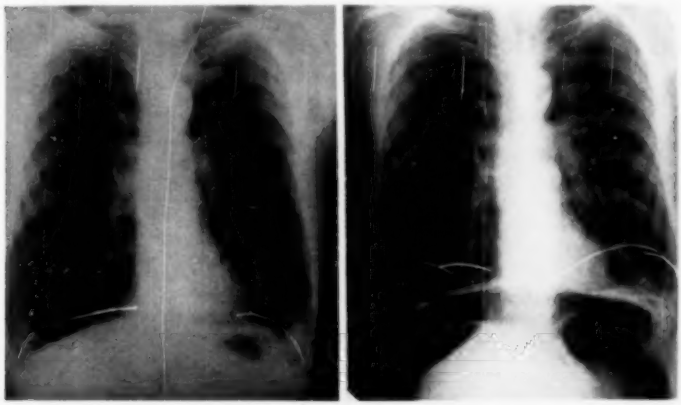

FIGURE 4. Case 4: From x-ray films showing limits of maximal diaphragm excursion before and after pneumoperitoneum treatment. For a description of technique, see legend, figure 2.

*Case 5 (V.H.C.):* This 57 year old white male's respiratory difficulties began in 1943 when he developed pneumonia following orchidectomy. After recovery he noted dyspnea, wheezing and a productive cough. These symptoms have persisted without seasonal variation. He has occasionally noted minimal ankle edema. A prolonged attempt at desensitization was unsuccessful. He has been unable to work for several years.

He was obviously severely emphysematous and quite dyspneic. His blood pressure was 122 75. Expiratory wheezes and a few crackling rales were heard at both bases. The heart size was normal. There was no cyanosis, clubbing of the fingers or edema. The three second vital capacity measured 1400 cc. He was given an initial pneumoperitoneum of 800 cc. of air. Four days later he was given 600 cc. of air, and volunteered

that his breathing was better. Further treatments have been carried out without difficulty. The dyspnea and wheezing have improved only moderately. Fluoroscopy shows improved movement of the diaphragm in contrast to pre-treatment studies. He continues to receive about 1200 to 1400 cc. of air every other week. On a recent visit to the clinic his three second vital capacity was 1850 cc. of air, an increase of 450 cc. over the pre-treatment figure.

While we believe we have helped this man, it is clear that he has received less benefit than the others. Since he has been treated a relatively short time, further improvement may occur. The patient is certain that for the first time since the development of symptoms, definite improvement in his breathing has been provided. Maximum inspiratory and expiratory diaphragm positions are shown in figure 5. Exercise olerance and vital capacity studies are indicated in the table.

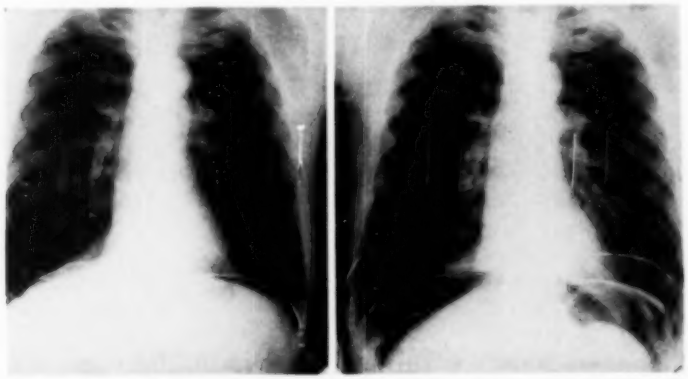

FIGURE 5. Case 5: From x-ray films showing limits of maximal diaphragm excursion before and after pneumoperitoneum treatment. For a description of technique, see legend, figure 2.

Two additional patients had such severe chest and shoulder pain following pneumoperitoneum that we were obliged to abandon this treatment. Both patients stated that, in spite of the pain, it was easier to take a deep breath while air was present in the peritoneal cavity. One patient, a 64 year old white male, had marked bilateral lower lobe bronchiectasis, in addition to severe bronchial asthma and emphysema. There were adhesions between the diaphragm and liver and spleen. In addition, fibrosis of the diaphragm had undoubtedly occurred in association with basilar infection and diaphragmatic pleuritis, and probably contributed in large measure to the immobility of the diaphragm and the pain which was produced when the diaphragms were elevated. The other patient, a 54 year old white male, had moderately severe emphysema with slight asthmatic wheezing of about two years duration. There was evidence of chronic basilar infection without bronchiectasis.

Antihistaminics and a prolonged de-sensitization program were of no help. Following the institution of pneumoperitoneum he experienced abdominal pain with every movement of the body, and suffered an aggravation of symptoms of hemorrhoids and an inguinal hernia.

### *Results*

The increase in vital capacity and improvement in exercise tolerance (as indicated by less arterial oxygen desaturation during exercise) following therapeutic pneumoperitoneum are shown in the table. Following therapeutic pneumoperitoneum, all patients were subjectively improved.

Vital capacity was significantly increased in all. (In two patients it was at least doubled). Arterial oxygen desaturation following standard exercise was uniformly less following treatment with pneumoperitoneum than before, but in two patients (cases three and five) this difference is within the limits of accuracy of the oximeter. Nevertheless, all changes, however slight, are in the direction of improved pulmonary function.

### *Discussion*

Results from the therapeutic use of pneumoperitoneum have been gratifying in five cases of pulmonary emphysema. Improved respiratory function and a surprising reduction in the severity and frequency of asthmatic attacks may occur. This has been observed before by Monaldi[3] and Rubin.[4]

In the past the procedure has been used extensively in the treatment of pulmonary tuberculosis. Our experience with pneumoperitoneum in emphysema indicates that it is safe and may be administered to out-patients.

Pain in the shoulders or lower chest is common after the initial injection of air. As a rule it is easily controlled with salicylates and codeine. However, it may persist. Indeed, it may force abandonment of the treatment, as occurred in two of our cases.

Pneumoperitoneum produces varying degrees of visceroptosis. It may aggravate hemorrhoids and distend hernia sacs. Usually the patient is willing to tolerate these discomforts because his breathing is so much better. Nevertheless, it would seem wise to repair herniae before undertaking treatment when this is feasible.

The contraindications to the use of pneumoperitoneum in the treatment of pulmonary emphysema are, in general, those which contraindicate its use in the therapy of pulmonary tuberculosis. These are discussed by Banyai.[10] Coronary artery disease and cardiac decompensation do not absolutely contraindicate pneu-

moperitoneum, but extreme caution with its use is mandatory when either is present.

Maximal benefit may be obtained only after many weeks of treatment, or it may become evident even before the initial injection is complete. The presence of chronic basilar pulmonary infection limits benefit obtained from this therapy. We feel, however, that each candidate should be given the benefit of a full therapeutic trial before he is rejected.

The mechanism whereby pneumoperitoneum affords relief to the emphysema patient is not precisely known. That increased vital capacity and diaphragmatic excursion are associated with improved oxygenation of the blood is apparent from this study. The exact significance o fimproved carbon dioxide elimination, acid-base regulation and pulmonary blood flow, which undoubtedly result from this procedure, awaits further study.

Pneumoperitoneum for emphysema represents symptomatic therapy, and should be employed only when no specific measures are available. It is recognized that environmental and psychological factors modify significantly the course of this disorder, particularly with respect to the asthmatic component. Only long term evaluation by repeated observation and testing will definitely establish the true worth of pneumoperitoneum as a treatment measure. However, it is a simple procedure, and clearly warrants further and more widespread application.

## SUMMARY AND CONCLUSIONS

1) The use of artificial pneumoperitoneum in the treatment of pulmonary emphysema may provide impressive symptomatic relief. Its use in seven patients is described.

2) Exercise tolerance and vital capacity may increase significantly following this procedure.

3) The physiological basis for the use of artificial pneumoperitoneum in pulmonary emphysema is discussed.

Grateful acknowledgement is made of the encouragement and helpful advice provided the authors by Dr. Hollis Johnson of Nashville, Tennessee.

## RESUMEN Y CONCLUSIONES

1) El uso del neumoperitoneo en el tratamiento del enfisema pulmonar, puede dar alivio sintomático impresionante.

2) La tolerancia del ejercicio y la capacidad vital pueden aumentar notablemente con este procedimiento.

3) Las bases fisiológicas para el uso del neumoperitoneo en el enfisema pulmonar se discuten.

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# Pulmonary Resection and Streptomycin in the Treatment of Pulmonary Tuberculosis*

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The possibility of treating pulmonary tuberculosis by the resection of the clinically involved area has intrigued interested minds since at least 1881 when Block made the first recorded attempt to perform such an operation. By 1948, 616 cases were reported in the literature.[1-7] Since that time, thoracoplasty failure, tuberculoma, bronchial obstruction with or without tension cavity, uncontrolled lower lobe disease, and symptomatic bronchiectasis have become generally accepted indications for pulmonary resection. Recent reports[5,8,9] demonstrate that the results obtained by resection can be improved through the coordinated use of streptomycin.

Our material consists of 24 cases, 17 white and seven colored males, whose operations were performed at Kennedy Hospital between November 1947 and September 1948, and who have been followed through October 1949. Of the 24 cases, there were 19 with far-advanced disease, including three negroes with recent tuberculous pneumonia. Three other patients had large single discrete tuberculomata. In all cases, the lesions were such as to satisfy, in our opinion, at least one of the indications for resection listed above. All patients received streptomycin for one week prior to operation and for two weeks thereafter. Fourteen patients had had previous courses of streptomycin, while the remaining 10 had not. The dosage of streptomycin generally employed was one gram daily, intramuscularly. All patients who had an upper lobe, or an equal amount of lung tissue removed, received thoracoplasty three weeks later, if possible, to prevent over-distension of the remaining lung tissue, improve pulmonary function, and to try to prevent

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a future flare-up of a small remaining tuberculous focus. Following lower lobe resection, phrenemphraxis was performed for similar reasons.

The early post-operative results showed apparent success, with sputum conversion in 18, or 75 per cent of the patients. Six patients had eight post-operative complications, consisting of three spreads of disease, two fistulae, two empyemata, and one transient non-specific pneumonitis. The fistulae occurred in the first two patients to have segmental resection, before it was realized that some refinements in technique were necessary for this operation. The following technical points in segmental resection seem worth stressing. The segmental plane is developed by sharp dissection, using great gentleness in handling the pulmonary tissue so that as much support of the bare lung as possible remains. All vessels and bronchi between segments are ligated. Some of the visceral pleura of the excised pulmonary segment is preserved to cover the bare area of the remaining lung tissue.

There was no immediate, or late, operative or tuberculosis mortality, but there was one death during the follow-up period, almost two years following the resection, from a self-administered overdose of morphine. This patient, fortuitously, was examined one week prior to his suicide and showed no reactivation of his tuberculosis.

Eighteen of the patients had pulmonary lesions that were stable for at least two months prior to operation. Among these, there were no immediate post-operative spreads. The remaining six were not considered stable at the time of surgery. These were patients with uncontrolled progressive disease, in whom the best that could be obtained, even following a course of streptomycin, was a precarious stalemate in which progression was halted but not reversed. It was thought best to operate without delay, for fear that the organisms would become resistant to streptomycin and that relapse would then occur. Of the six patients in this category, three suffered post-operative spreads. Two of the spreads were resolved promptly by streptomycin and temporary collapse measures. The remaining patient, a negro convalescing from tuberculous pneumonia is still in the hospital under treatment, and his prognosis appears to be no better than it was prior to surgery. The above data suggest that the less stable the disease, the greater the risk of the operation.

The type of operation used, varied. It was found at the time of surgery that the disease in 11 of the 24 patients had a segmental distribution. For such cases, in order to preserve the uninvolved segments in each lobe, segmental resection rather than lobectomy was performed. In two cases it was found possible to do segmental

resection during the same operation that the remainder of the lung was decorticated, with good results. Where the lobe was too extensively involved, the entire lobe was, of course, removed. Spreads occurred in two of the 10 patients who had lobectomy, in one of the four who had a lobectomy and additional segmental resection, but in none of the seven who had segmental resection alone or segmental and decortication. These results indicate to us that with suitable surgical technique the extent of the disease is of greater importance than the type of resection employed and that the preservation of the maximum amount of normal lung tissue should be a principal consideration.

It is generally accepted that, whatever the reasons, colored people are less resistant to tuberculosis than white. In our series of seven colored and 17 white males, one negro had an immediate post-operative spread, as did two white patients. The latter, however, with treatment quickly controlled their spreads; the former has thus far failed to do so. It is also of interest that, during the period of follow-up only one white patient, out of the 17, has relapsed and is still in the hospital. On the other hand, two negroes have relapsed, making a total of four, out of seven, still hospitalized and requiring treatment. Our especially poor results in two out of the three colored patients with recent tuberculous pneumonia adds to our feeling that in negroes, particularly, pulmonary resection is hazardous unless the lesions are definitely stable.

The condition of the contralateral lung appears to be of importance. Seven of the 24 cases had a minimal, inactive, but obvious lesion on the contralateral side. Two of these seven showed post-operative spreads, whereas only one out of the 17 unilateral cases showed a spread. In addition, a middle-aged white male for whom resection was performed because of thoracoplasty failure, developed a reactivation of his contralateral lesion 10 months after his operation. The lesion disappeared after treatment with streptomycin and pneumoperitoneum, only to reappear again in three months. He is still in a hospital under treatment. It would appear, therefore, that contralateral lesions, even when minimal and inactive, form an additional factor to be evaluated in considering pulmonary resection.

The question of the relation of previous courses of streptomycin to complications also came under consideration. Of the 10 cases considered sufficiently stable to withstand resection without prior courses of streptomycin, there were no post-operative spreads, but there were two relapses, and three of these 10 patients are still in a hospital receiving treatment. Of the six cases who had received long courses, 120 days, of streptomycin prior to resection, there were no spreads, no relapses, and none whose disease is still

active at this time. However, of the eight cases who had received short courses, 42 days, of streptomycin prior to resection, there were three post-operative spreads, one relapse, and two of these patients are still in a hospital under treatment. From the above, it would appear justifiable to give as long a course of streptomycin as is necessary to produce stabilization.

Three of our patients suffered rather unusual complications which we mention merely for the sake of completeness. One patient with tuberculoma of the lung developed iritis one month following surgery, and a similar patient with tuberculoma developed a tuberculoma of the larynx six weeks following surgery. The relationship of these complications to the operations is questionable. At any rate, both patients responded satisfactorily to the appropriate treatment. A third patient has developed recurrent tuberculous chest wall abscesses at the site of the operation. This patient's sputum is negative and his pulmonary lesion appears to be well-controlled, but he is still hospitalized, and he is, therefore, described as "active."

*Discussion*

We believe that this study permits a better understanding of those lesions of pulmonary tuberculosis for which resection is now applicable with the help of streptomycin. It seems to us that stability is the most vital factor in the evaluation of a patient for this treatment. The results we obtained in our negro patients make us feel that where poor resistance is believed to be present, the requirement of stability should be especially stringent. Prior courses of streptomycin in themselves do not, we believe, predispose to complications. Our patients who received such courses were, without exception, patients with acute progressive disease for whom no surgery was possible until they had had streptomycin. But, because with streptomycin constitutional symptoms disappear promptly and patients gain weight rapidly, it becomes difficult to decide when sufficient stability has been reached to permit surgery. This difficulty in evaluation should yield to further experience, but in the meantime, our results suggest that one should play safe and favor the more prolonged courses. If combined streptomycin and para-aminosalicylic acid therapy is utilized, then the danger of the premature development of resistance by the tubercle bacilli may be decreased. Other factors that should be considered in the evaluation of a patient for resection are disease on the contralateral side and the amount of lung that needs be resected. Our experience is not sufficiently great, however, to enable us to assign the proper weight to the latter. It must be perfectly clear, however, that pulmonary resection has not de-

creased the importance of bedrest, either prior t osurgery or during the period of convalescence. Tuberculosis must be considered as a disease with widespread foci, while pulmonary resection by its very nature is merely an attempt at the extirpation of the most grossly involved area. In addition, the prompt and effective treatment of such complications as fistula, empyema, spreads, and pneumonitis is possible only in patients who remain under medical care. Neither must resection be considered a substitute for, or in competition with, other forms of collapse therapy, especially those forms such as thoracoplasty and pneumothorax, which have demonstrated their value over a period of many years. It may be considered in certain cases where such collapse procedures have failed or, in the light of previous experience, might be predicated to fail.

The results achieved in our series of patients seem to us to be remarkably good. They certainly have encouraged us to continue with this form of treatment in suitable cases. As of October 12, 1949, out of the 24 patients treated, 10 were arrested, seven apparently arrested, and two were quiescent. Four patients were considered active, and one was dead as a result of suicide after having been arrested for more than a year.

## SUMMARY AND CONCLUSIONS

1) Pulmonary resection with concomitant streptomycin therapy, is a valuable method of treatment for suitable types of pulmonary tuberculosis.

2) Stability appears to be the most vital factor in the evaluation of a patient for this procedure.

3) Preliminary courses of streptomycin make surgery feasible for some of the poor risk cases. Correct evaluation of stability, however, is thereby made more difficult.

4) Resistance, contralateral disease, and the amount of lung to be resected are other factors that appear to be of importance in the evaluation of suitable cases.

5) Resection has not decreased the necessity of prolonged bedrest and treatment but has made it more important and essential. Prompt active treatment of complications is possible only in cooperative patients who remain under medical care.

6) Resection is not considered to be a substitute for, or to be in competition with, recognized collapse procedures. It has been used where these procedures have failed or could be predicated to fail.

## RESUMEN Y CONCLUSIONES

1) La resección pulmonar con estreptomicino terapia concomitante es un buen método para tratar casos adecuados de tuberculosis.

2) La estabilización parece el factor vital más importante en la valuación de un enfermo para este procedimiento.

3) El tratamiento previo con estreptomicina hace factible la cirugía para los casos más deficientes. La valuación correcta de la estabilización, sin embargo, es por eso más difícil.

4) La resistencia, la enfermedad contralateral y el volumen del pulmón por resecarse, son los otros factores que parecen de importancia para estimar los casos adecuados.

5) La resección no ha hecho disminuir la necesidad de reposo prolongado y tratamiento, sino que los hace más importantes y esenciales. El tratamiento inmediato y activo de las complicaciones es posible en enfermos que cooperen para permanecer bajo tratamiento médico.

6) La resección no debe considerarse un substituto de, o competidor de los procedimientos reconocidos de colapso. Se ha usado donde estos procedimientos han fracasado y pudo predecirse que fracasarían.

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# Middle Lobe Disease*

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This paper is based on 19 patients who had right middle lobectomy for disease limited to the middle lobe, 16 of whom were treated in the past year. The apparent increase in frequency of recognition of disease limited to the middle lobe prompted this review which has brought to light several interesting findings. Ten of the patients had bronchiectasis limited to the middle lobe, six had lung abscess, and three had tuberculosis. Their ages ranged from five to 68 years with a medium of 38 years.

*Etiology*

As has been pointed out by Graham and others, the reason inflammatory pulmonary disease limits itself to the right middle lobe is an anatomic one. The lymph nodes are so arranged about the middle lobe bronchus near its origin that only moderate enlargement of them will cause complete bronchial occlusion. Such an arrangement is not present in any other portion of the lung.

When an inflammatory process involves the right middle lobe, complete bronchial occlusion often follows by enlargement of peribronchial lymph nodes, preventing bronchial drainage. The immediate result is a swollen, dense middle lobe, often with early abscess formation. If the acute process subsides and the bronchus reopens, bronchiectasis may be present. Fourteen of our 19 patients gave a history of acute onset of their disease. All 10 patients with bronchiectasis had chronic cough productive of purulent sputum. Three of the 10 had had hemoptysis. The illness of all six patients with lung abscess began as an acute pneumonic process characterized by chest pain, productive cough and fever. Two had hemoptysis.

The three patients with tuberculosis of the right middle lobe had acute onset but the acute episodes had subsided when we saw them. The sputa of the two adult patients were negative for tubercle bacilli while that of the third patient, a five year old boy, was not examined.

One of the most striking findings in the review of this small series of cases was the relatively normal appearance of regular frontal x-ray films of the chest in patients with bronchiectasis

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limited to the middle lobe. The usual x-ray report was increased bronchovesicular markings on the right side. Adequate bronchograms with five lobe filling, of course, establishes the diagnosis.

Of the six patients with abscess, the x-ray interpretation of three was consolidation of right middle lobe; of two, consolidation with abscess formation; of one, atelectasis with abscess formation. The usual bronchoscopic findings in these patients were constriction of the right middle lobe orifice and pus coming from that orifice.

### *Therapy Without Surgery*

No attempt was made to treat the patients with bronchiectasis by medical therapy. The six with abscess of the right middle lobe were all given blood transfusions in sufficient amount to raise the hematocrit to 50 per cent. Crystalline penicillin in dosage of 100,000 units every three hours was given. Five of the patients had symptomatic improvement on this regimen, but none showed signs of clearing of the diseased right middle lobe. The sixth patient spiked a fever to 104 degrees F. daily and went progressively downhill in spite of therapy until his diseased middle lobe was removed.

The diagnosis of tuberculosis was not made in any of the three patients with tuberculosis of the right middle lobe, although repeated sputum examinations for tuberculosis were made in two of them. Penicillin had no effect on these patients.

### *Operative Technique*

The operative technique for right middle lobectomy is essentially the same as for the removal of other lobes. However, because of the arrangement and intimacy of the lymph nodes about the middle lobe bronchus and artery due to inflammatory changes, it may become hazardous to persist in the isolation of the individual hilar structures in the usual fashion. When this problem arises, it has been found expeditious to place a clamp across the hilar structures of the middle lobe and cut distal to the clamp, removing the lobe without isolation of the individual structures. The clamp is then removed and the vessels and bronchus caught individually and treated in the usual manner. No complications have arisen from this technique in the few instances that it has been used.

### *Results*

Of the 10 patients with bronchiectasis of the right middle lobe, all had an excellent result. No patient had empyema or other complications. Of the six patients with abscess of the right middle lobe, four had an excellent result. One has had two episodes of right chest pain with fever and infiltration in the anterior segment

of the right upper lobe as manifested by x-ray inspection. Penicillin was effective in treatment in each instance.

The second patient, a 66 year old man who developed right middle lobe abscess while in a general hospital being treated for bilateral gangrene of the feet due to frostbite, developed a localized empyema two months after operation. The space obliterated a short time after drainage. Thus, this complication did not prove to be a serious one. Of the three patients with tuberculosis of the right middle lobe, two had excellent results. One, a five year old boy, had spread to left upper lobe which cleared with streptomycin therapy.

*Case Histories*

R.M., a white female of 28 years, was admitted April 11, 1949 and discharged April 30, 1949. Two months before admission she developed fever, cough, dyspnea and pain in right side of her chest. Penicillin therapy relieved symptoms but nonproductive cough persisted. Two days before admission fever and right lower chest pain recurred and cough was productive of a small amount of thick yellow sputum. There were 4,210,000 erythrocytes with hemoglobin of 11 grams, and 19,200 leucocyte cells. Bronchoscopy on April 12, 1949 revealed pus exuding from the middle lobe orifice. Right middle lobectomy was done on April 19, 1949. Recovery was uneventful and she was discharged on the eleventh post-operative day. Pathological diagnosis was lung abscess from unresolved pneumonia.

J.K., a white male of 62 years, was admitted on September 4, and discharged on September 26, 1948. He was well until four weeks before admission when he developed fever, dyspnea, cough productive of rusty sputum and pain on the right side of his chest. He received penicillin therapy with some relief of symptoms, but fever, dyspnea, and productive cough persisted. On admission he had 3,990,000 erythrocytes, hemoglobin 65 per cent and 18,900 leucocyte cells. His temperature reached 103 degrees F. daily and his condition became worse in spite of blood transfusions, penicillin, and streptomycin therapy. Right middle lobectomy was done on September 9, 1948. He made a slow recovery and was able to return to work after several months.

A.R. This 35 year old white female school teacher was well until January 1949. Annual chest x-ray inspections were required by her employer. In January 1949, she developed an upper respiratory infection with slight cough. One month later she had a small amount of blood streaked sputum. X-ray inspection of the chest at that time showed evidence of pneumonitis in the right lower lung field. She was treated with penicillin without change in the appearance of the shadow. She was asymptomatic on admission April 3, 1949. Six sputum examinations were negative for tubercle bacilli. Bronchoscopy revealed constriction of the right middle lobe orifice. Right middle lobectomy was done on April 7, 1949. She made an uneventful recovery and was discharged on the twelfth post-operative day. The pathological diagnosis was tuberculosis with cavitation.

Father H., a white priest of 38 years, was admitted on December 14, 1948 and discharged January 2, 1949. He had cough with morning expectoration of purulent material for years with pneumonia in November 1948.

Bronchoscopy revealed bronchiectasis and atelectasis of the right middle lobe. Right middle lobectomy was done on December 17, 1948 with uneventful recovery. The pathological diagnosis was bronchiectasis.

## SUMMARY

The anatomic arrangement of lymph nodes about the middle lobe bronchus, the moderate enlargement of which produces bronchial occlusion, appears to be the reason for inflammatory disease limiting itself to the right middle lobe.

Most patients with inflammatory disease limited to the middle lobe give a history of an acute pneumonic onset, the symptoms of which never clear completely or recur after the cessation of penicillin therapy.

The changes in the frontal x-ray film of the chest are often negligible in patients with bronchiectasis limited to the middle lobe and the symptoms are often much more severe than one might expect from the amount of pulmonary tissue involved.

The technique of dividing the hilar structures of the middle lobe distal to a clamp, removing the clamp, and then treating the vessels and bronchus individually has been found to give satisfactory results when adherent lymph nodes made the usual isolation and individual ligation method too hazardous.

Right middle lobectomy is the only satisfactory method of treatment of inflammatory lesions of the middle lobe with bronchial obstruction which fail to clear by medical therapy.

## RESUMEN

La situación anatómica de los ganglios linfáticos alrededor del bronquio del lóbulo medio que por su crecimiento puede producir oclusión bronquial, parece ser la razón de que la enfermedad se limite al lóbulo medio derecho.

La mayoría de los enfermos con enfermedad inflamatoria limitada al lóbulo medio, tienen historia de principio agudo neumónico, cuyos síntomas nunca se aclaran por completo o recurren al cesar el tratamiento con penicilina.

Las alteraciones que pueden notarse en la película radiográfica posteranterior a menudo son insignificantes en los enfermos con bronquiectasis limitada al lóbulo medio y los síntomas son mucho más severos de lo que uno esperaría por el volumen de pulmón comprometido.

La técnica de seccionar las estructuras hiliares del lóbulo medio distalmente a un clamp, retirar ésta y entonces tratar los vasos y el bronquio individualmente, se ha encontrado que dá resultados satisfactorios cuando los ganglios adherentes hacen el asilamiento y la ligadura individual demasiado peligrosos.

# EDITORIALS

## PULMONARY SARCOIDOSIS

Sarcoidosis of the lung is one of the most elusive, protean and capricious clinical entities. As it is pointed out in the excellent article of Oblath and Farber in this issue, this condition has been recognized with increasing frequency in recent years. The reason for this is a prevalent better diagnostic consciousness rather than an increase in the incidence of the disease.

The number of synonyms to sarcoid lesions reflects the effort and lack of consensus concerning their clinical status. Common manifestations of sarcoidosis have been recorded under the following technical terms: (1) Lupus pernio. (2) Benign lupoids. (3) Heerfordt syndrome or uveoparotid fever. (4) Benign lymphogranulomatosis. (5) Osteitis fibrosa cystoides. (6) Paratuberculosis. (7) Generalized sclerosing tuberculous macrocytic (giant cell) hyperplasia. (8) Reticuloendotheliosis. (9) Chronic infectious epithelioid cell reticuloendotheliosis. (10) Non-caseating tuberculosis. In addition to these terms, the following represent the same histopathologic entity: (1) Miliary lupoid. (2) Tuberculosis indurativa lupoides. (3) Subcutaneous sarcoids of Darier and Roussy. (4) Angiolupoid of Brocq and Pautrier.

It has been long known that histopathologic findings play an important role in the clinical identification of this condition. Most conspicuous of these is the "naked tubercle," so called on account of the scarcity of lymphocytes at the periphery of these granulomatous structures as compared with the tubercle seen in tuberculosis. The sarcoid tubercle consists of palely staining, polygonal epithelioid cells which may show a mosaic pattern in the center and a concentric arrangement at the periphery. Within the cluster of epithelioid cells, giant cells of the Langhans type are common but not always present. The number of nuclei in these cells may be as high as 30. Sometimes, the giant cells of sarcoid contain irregularly shaped or oval, laminated, deeply staining basophilic inclusions of various sizes, with asteroid projections. Healing of the sarcoid tubercle may ensue by complete resorption or by fibrosis.

Postmortem examination of the lung affected with sarcoidosis reveals the following pertinent findings. From pin point to pea-sized nodules may be seen on the surface. On palpation, the lung feels firm and nodular. The lung may be contracted due to fibrosis. The cut surface shows nodules varying in size from 2 to 5 mm.

Cavity formation is infrequent but cavities of medium and even large size have been observed on necropsy in patients with sarcoidosis and without tuberculosis. The hilar lymph nodes are enlarged or they may be reduced in size by fibrotic induration. On histologic inspection, one finds loss of the parenchyma in consequence of sarcoid nodules; also, net-like, string-like or massive areas of fibrosis. Fibrosis may cause narrowing of the lumen or complete obliteration of capillaries, small blood vessels, bronchioles and bronchi. In some instances, bronchiectasis results from the pulmonary fibrosis; in others, compensatory emphysema may be noted. Also, the pleura may be affected. In rare instances, pleural effusion develops on one side or, as it happened in one of the author's cases, consecutively on both sides.

Possible complications of pulmonary sarcoidosis include spontaneous pneumothorax, paralysis of the phrenic nerve due to pressure of enlarged mediastinal lymph nodes, purpura, toxic erythema and erythema nodosum. The latter is nontender; it is not associated with pruritus and lasts for a few weeks. Sarcoid nodules may develop in other vital organs. The function of the latter may be disturbed by the replacement of specific tissues by sarcoid nodules or by the pressure of sarcoid masses. Involvement of the peripheral superficial lymph nodes occurs some time during the course of sarcoidosis in nearly 100 per cent of the cases. The implicated lymph nodes are enlarged, often to a considerable size, and are firm, rubbery, nontender and nonadherent to the surrounding structures. Retrobulbar localization of the disease may cause unilateral exophthalmos. Central nervous system involvement may lead to symptoms of encephalitis or cranial nerve paralysis. Findings suggestive of diabetes insipidus may result from sarcoid changes in the hypophysis. Arrhythmias, conduction defects and myocardial failure may follow sarcoid infiltration of the heart muscle. Strain and failure of the right side of the heart may result from extensive perivascular pulmonary fibrosis secondary to sarcoidosis. Cardiac decompensation is made worse by the pressure of enlarged hilar and mediastinal lymph nodes upon the auricles and the large blood vessels. Enlargement of the liver and the presence of icterus are more readily attributed to diseases other than sarcoidosis. Splenomegaly with leucopenia and thrombocytopenia may suggest Banti's disease, aplastic anemia or essential thrombocytopenia. There may be a spontaneous complete disappearance of splenomegaly during the course of the disease. Involvement of the kidneys may simulate the clinical picture of subacute glomerulonephritis with azotemia. Cases are on record where sarcoidosis led to the development of Still's syndrome.

As it has been aptly pointed out in the paper of Oblath and

Farber in this issue, roentgenologic manifestations of thoracic sarcoidosis may be encountered in four forms: (1) Massive, lobulated, soft-appearing enlargement of the hilar and paratracheal lymph nodes. The roentgenogram reveals a butterfly appearance or the so-called potato nodes. The lymph node involvement is bilateral and symmetrical. Rarely, however, the disease is localized in one hilar region. In a considerable percentage of cases, there is a pronounced enlargement of the paratracheal lymph nodes on the right side as compared with the opposite side. This finding may be only apparent or may represent actually greater involvement of these structures on the right side. It may be apparent on account of the better visual accessibility of mediastinal structures on the right side. It may be real, for the right lung being larger in volume than the left, it is supplied with a more abundant lymphatic system, including corresponding lymph nodes. Limited enlargement of hilar and mediastinal lymph nodes is readily demonstrable in x-ray films taken in right or left oblique projection or with the aid of the Bucky diaphragm or tomograph. (2) Enlargement of the hilar and mediastinal lymph nodes in sarcoidosis may be associated with peribronchial, perivascular and interlobular infiltration and fibrosis which give the appearance of radiation from the hilum toward the periphery or bring about a net-like reticulation in the lung fields. (3) The most frequently seen and generally accepted "typical" pulmonary sarcoidosis is represented by scattered, fine, micronodular densities. This roentgenologic picture, together with the rather slow course of the disease, prompted older clinicians to refer to it as granulie froide, granulie discrete, miliaris discrete and tuberculids of the lung. It is interesting to find that the apex and the base of the lung are relatively free of these nodules. (4) Pulmonary sarcoidosis may manifest itself in irregularly shaped, unevenly distributed or localized, patchy infiltration which is similar to tuberculous lesions and to bronchopneumonia of other bacterial, rickettsial, viral or parasitic origin.

The course of sarcoidosis is unpredictable. It may last from several months to as long as 20 years. Enlarged hilar and mediastinal lymph nodes may completely recede to their normal size. Also, extensive pulmonary involvement may clear entirely. Such train of events may be anticipated in about one-third of the cases. Retrogression of pathologic changes, however, does not necessairly mean recovery. For reasons unknown, clinically satisfactory course of the disease may be interrupted by a flare-up in the lung or in some other part of the body. Bacilliferous (open) pulmonary tuberculosis is a frequent sequel in these patients from several months to several years after the onset of sarcoidosis.

The various methods and drugs advocated for the management of sarcoidosis are the unmistakable, though regrettable, expression of the fact that there is no uniformly potent means for the treatment of this disease. There have been trials at curing sarcoidosis with ultraviolet irradiation, arsenicals, iodides, vitamin C, gold salts, tuberculin, hyperpyrexia and radium. Reports are contradictory concerning the benefits of x-ray therapy. Calciferol and dihydrotachysterol have been recorded as of value in the cutaneous and pulmonary forms of sarcoidosis. Recently, favorable results have been observed following the administration of nitrogen mustard, methyl bis (beta chloroethyl) amine hydrochloride. Also, ethyl chaulmoograte has been endorsed by outstanding clinicians as a useful therapeutic agent in sarcoidosis. The final acceptance of any of these measures requires more extensive clinical experience with them.

A. L. B.

## PULMONARY EMPHYSEMA

This condition has long been the bane of physicians everywhere. When chronic hypertrophic emphysema is well established it is irreversible. Therefore, there is no hope of curing the condition by any form of treatment. Often, emphysema sufferers become totally incapacitated even to the point of being unable to take a few steps. Usually the incapacity is first manifested by slight shortness of breath on exertion. It may then slowly increase over months or years until no work is possible. Later the slightest movements of the body may result in difficult respiration. Many attempts have been made by physicians to devise methods to prevent the progressive development of emphysema and also to overcome various degrees of incapacity in well established cases.

For patients who have severe bronchial symptoms with tenacious sputum, drugs such as potassium iodide have long been used to liquefy the bronchial secretions. Sulfonamides and antibiotics have been administered by all known methods to overcome infections. Bronchoscopy has been employed to remove obstructions if found, and tenacious bronchial accumulations, etc. When bronchial asthma coexists, attempts have been made to find its cause, particularly if it is on an allergic basis, then to desensitize or avoid substances thought to be responsible. During attacks such drugs as adrenalin, ephedrine and aminophylline have been used to relieve the bronchial spasm. In some cases the inhalation of 70 to 100 per cent oxygen by mask for 20 to 30 minutes two or three times a day has given temporary relief. In extremely severe cases, continuous oxygen therapy has been employed for several weeks at a time or until relief from dyspnea and adequate restoration of respiratory function is established.

Since overdistention of the lungs depresses the diaphragm so it loses its normal contour and much of its excursion during respiration, it has long been thought that any procedure which would elevate the diaphragm to its usual level and restore its movements should result in at least partial relief of symptoms. Alexander and Kountz employed an especially constructed abdominal support to elevate the diaphragm which relieved symptoms. Gordon constructed supports which elevated the diaphragm from 1 to 3.5 cm. He observed that the sudden motion of the diaphragm during coughing was decreased when it was in this elevated position. Barach recommends an elastic abdominal belt to be worn during the day. He also teaches patients to place the palms of both hands immediately below the costal margin and push inward and upward during the latter third of expiration to aid in the expulsion of the trapped pulmonary air. If this is done for one or two minutes

three times each day, it often reduces dyspnea and improves the excursion of the diaphragm. Temporary interruption of the phrenic nerve has also been employed.

In this issue of *Diseases of the Chest*, Furman and Callaway report encouraging results from the use of artificial pneumoperitoneum. This has been used for more than 25 years in the treatment of pulmonary emphysema. In fact, Reich in 1924 and others have observed relief of symptoms from this treatment. However, a considerable number of workers did not proceed methodically and therefore observed no benefit. No attempt was made to elevate the diaphragm to a sufficiently high level and maintain it in this position by adequate amounts of air frequently administered into the peritoneal cavity. An occasional injection of 300 or 400 cc. of air could hardly be expected to have much effect on the position of the diaphragm. Encouraged by the results reported by such workers as Reich and Banyai, Furman and Callaway proceeded to study the various aspects of emphysema and to determine why restoration of position and excursion of the diaphragm should result in benefit to patients. Although their number of cases is small and they wisely present their work as a preliminary report, some of their results are impressive. They have restored the diaphragms of their patients to approximately normal levels with satisfactory excursions. This has resulted in increased vital capacity and improvement in exercise tolerance. All of their patients were subjectively improved, some even restored to reasonably good working capacities. These findings have stimulated the authors to continue their observation and should encourage other physicians to study this method.

The extensive investigations on pulmonary function now in progress in such centers as New York City, Rochester, New York, Saranac Lake, New York, Philadelphia and the Veterans Administration Hospital in Minneapolis are contributing to our knowledge of emphysema which may be advantageous in treating this condition.

J. A. M.

## *First International Congress on Diseases of the Chest*

On the seventeenth of this month the First International Congress on Diseases of the Chest will open in Rome, Italy. The Congress is sponsored by the Council on International Affairs of the American College of Chest Physicians and the Carlo Forlanini Institute of Rome, where the scientific sessions are to be held. More than one hundred speakers from countries all over the world will present scientific papers on subjects covering the most recent developments in the treatment of diseases of the chest. In addition to the scientific sessions on Monday, Tuesday, Wednesday and Thursday, September 18 through 21, a clinical-pathological conference will be presented on Thursday afternoon. A program of motion picture films on various techniques in the treatment of diseases of the chest will also be shown each day.

Two executive sessions to which all officials of the College attending the Congress are invited, have been scheduled for the purpose of discussing activities of the College. The opening executive session will be held on Saturday, September 16 and the closing executive session on Friday, September 22.

The Inaugural Ceremonies of the Congress will be held on Sunday, September 17 at the Palazzo Venezia, and a formal banquet and ball will be held on Thursday evening, September 21. Other entertainment and tours of Rome and the surrounding country have also been planned.

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## *Sixteenth Annual Meeting American College of Chest Physicians*

### ANNUAL MEETING OF THE BOARD OF REGENTS

The Board of Regents of the College held its annual meeting on Thursday afternoon, June 22, at the St. Francis Hotel, San Francisco, and met again on Sunday afternoon, June 25. The following Board members, council and committee chairmen, and guests were present:

James H. Stygall, Indianapolis, Indiana, Chairman, presiding
Manuel Albertal, Buenos Aires, Argentina
Robert J. Anderson, Washington, D. C.
Carl C. Aven, Atlanta, Georgia
Andrew L. Banyai, Milwaukee, Wisconsin
Otto L. Bettag, Chicago, Illinois
Benjamin L. Brock, Downey, Illinois
Miguel Canizares, Quezon City, Philippine Islands
Seymour M. Farber, San Francisco, California
Alvis E. Greer, Houston, Texas
Edward W. Hayes, Monrovia, California
Charles M. Hendricks, El Paso, Texas
David W. Heusinkveld, Cincinnati, Ohio
Robert B. Homan, Jr., El Paso, Texas
William A. Hudson, Detroit, Michigan

Chevalier L. Jackson, Philadelphia, Pennsylvania
Hollis E. Johnson, Nashville, Tennessee
Edwin R. Levine, Chicago, Illinois
Louis Mark, Columbus, Ohio
Donald R. McKay, Buffalo, New York
Francisco Menendez, Havana, Cuba
Leslie Mullen, Calgary, Alberta, Canada
Jay Arthur Myers, Minneapolis, Minnesota
James M. Odell, The Dalles, Oregon
J. Winthrop Peabody, Washington, D. C.
Karl H. Pfuetze, Cannon Falls, Minnesota
Joseph C. Placak, Cleveland, Ohio
Eli H. Rubin, Bronx, New York
William R. Rumel, Salt Lake City, Utah
Italo F. Volini, Chicago, Illinois
William C. Voorsanger, San Francisco, California
David H. Waterman, Knoxville, Tennessee

Murray Kornfeld, Chicago, Illinois, Executive Secretary
Harriet E. Lumm, Chicago, Illinois, Assistant Secretary
Samuel N. Turiel, Chicago, Illinois, Assistant Secretary

The following reports were presented:

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## REPORT OF THE TREASURER

DECEMBER 31, 1949

| | | | |
|---|---|---|---|
| INCOME: | | | |
| New Membership Fees | | $10,620.00 | |
| Dues | | 56,090.03 | |
| Sales: | | | |
| Advertising | $13,440.57 | | |
| Subscriptions | 8,942.16 | | |
| Directory | 40.00 | | |
| Fellowship Keys | 254.63 | | |
| Medical Book Service | 976.32 | 23,653.68 | |
| Postgraduate Courses | | 8,619.95 | |
| Interest on U. S. Govt. Bonds, Series "G" | | 582.50 | |
| TOTAL INCOME | | | $99,566.16 |
| EXPENSES: | | | |
| Salaries | | $22,795.24 | |
| Printing Diseases of the Chest | | 24,560.37 | |
| Additional Cost for Printing Special Issue | | 3,000.00 | |
| Annual Meeting | | 5,142.00 | |
| European Trip of Executive Secretary | | 3,340.67 | |
| Posting of the Journal | | 2,974.30 | |
| Postage and Shipping | | 2,361.23 | |
| Rent and Electricity | | 4,546.59 | |
| Officers and Committee | | 2,936.15 | |
| Printing and Engraving | | 2,974.18 | |
| Office Expense | | 1,370.98 | |
| Telephone and Telegraph | | 1,329.09 | |
| Editor of the Journal | | 650.00 | |

| | | |
|---|---|---|
| Semi-Annual Meeting — Board of Regents | 595.06 | |
| Traveling — Executive Secretary | 1,392.51 | |
| Certificates | 462.28 | |
| Secretary to Chairman of Board of Regents | 300.00 | |
| Secretary to the President | 300.00 | |
| Library | 83.25 | |
| Annual Award | 174.83 | |
| Auditing | 175.00 | |
| ULAST Meeting | 1,021.23 | |
| Public Relations | 785.85 | |
| Postgraduate Courses | 5,733.36 | |
| Depreciation | 444.48 | |
| Miscellaneous Expense | 35.80 | |
| TOTAL EXPENSES | | $89,484.45 |
| NET INCOME FOR THE YEAR | | $10,081.71 |

Despite the increase in the services rendered to the College members and the added expenses necessary to carry on these services, I am pleased to report that the College closed the year 1949 with a surplus of $10,081.71. Ten thousand dollars of this amount was invested in U. S. Savings Bonds, Series "G".

The books were audited by the La Salle Audit Company of Chicago.

**FINANCIAL STATEMENT**

June 1, 1950

| | | |
|---|---|---|
| GENERAL FUND: | | |
| Cash in First National Bank of Chicago | $57,382.65 | |
| Cash on Hand | 25.00 | |
| U. S. Savings Bonds — Series "G" | 30,000.00 | |
| TOTAL GENERAL FUND | | $ 87,407.65 |
| RESEARCH COUNCIL FUND: | | |
| Cash in First National Bank of Chicago | $ 2,570.63 | |
| U. S. Savings Bonds, — Series "G" | 41,700.00 | |
| TOTAL RESEARCH COUNCIL FUND | | 44,270.63 |
| LIFE MEMBERSHIP FUND: | | |
| Cash in First National Bank of Chicago | $ 235.00 | |
| U. S. Savings Bonds — Series "G" | 3,300.00 | |
| TOTAL LIFE MEMBERSHIP FUND | | 3,535.00 |
| TOTAL NET WORTH | | $135,213.28 |

BENJAMIN L. BROCK, M. D.
Assistant Treasurer

## REPORT OF THE COMMITTEE ON MEMBERSHIP

June 1, 1950

As of June 1, 1950, there were 3129 members in the College, and 150 applications for membership were pending investigation. This is an increase of 226 new members admitted into the College during the past year. Of the 3129 members, 2185 are Fellows of the College, 203 are Associate Fellows, and 741 are Associate Members. Our increase represents 125 Fellows, 28 Associate Fellows and 73 Associate Members.

In the United States of America and its possessions, there are 2100 members, while in countries outside of the United States, there are 1029 members. Our membership in other countries is distributed in 60 countries. Since the report of the Membership Committee in 1949, new members have been admitted from five additional countries.

CHEVALIER J. JACKSON, M. D.
Chairman

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## REPORT OF THE COUNCIL ON POSTGRADUATE MEDICAL EDUCATION

### POSTGRADUATE COURSES IN DISEASES OF THE CHEST

| | Enrollment | | | |
|---|---|---|---|---|
| City | 1948 | 1949 | 1950 | 1951 |
| Philadelphia | 62 | 44 | 47 | |
| Chicago | 44 | 38 | Oct. 16-20 | |
| Minneapolis | | 28 | | |
| New York | 76 | 86 | Nov. 13-18 | |
| Nashville | | | | Jan. 22-26 |
| San Francisco | 43 | 71 | | Feb. 13-17 |
| | 225 | 267 | | |

J. WINTHROP PEABODY, M. D.
Chairman

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## REPORT OF THE COMMITTEE ON CHEST DISEASES IN PENAL AND MENTAL INSTITUTIONS

There continues to be a slow but persistent effort to establish and maintain good epidemiology and therapeutics in chest diseases in penal and mental institutions. Several states have commendable programs. The committee is especially appraised of the work done in Illinois. The twelve (12) institutions for the mentally ill and the eleven (11) educational (blind, deaf, etc.) and correctional (boys' schools, girls' schools, etc.) with a total population of approximately 49,000 have routine entrance and semi-annual follow-up chest x-rays.

Any patient with questionable x-ray findings is placed in an observation ward for complete clinical work-up. Mental patients with active tuberculosis are isolated in separate units (12). Only a few patients with tuberculosis have been detected in the educational and correctional in-

stitutions. These are transferred to public sanatoria or occasionally isolated within the hospital facility.

Therapy to date includes bed rest, antibiotics and minor collapse procedures. Facilities for thoracic surgery are being established. The program has had the benefit of guidance by a non-political medical advisory committee. It is the general concensus of the committee to decontrol the multiple treatment units and establish one or two large metropolitan (Chicago - St. Louis) medical centers for obvious reasons. At the present time there are approximately 2,000 active cases of tuberculosis.

The Tuberculosis control program outlined above also includes approximately 10,000 institutional employees of the Department of Public Welfare. The disclosed cases amongst the personnel are referred to public or private agencies.

The Illinois Penal System, a unit of the Department of Public Safety, has a somewhate similar control program. A geographically central tuberculosis hospital houses all inmates with active tuberculosis. Until recently all thoracic surgery was done there.

The Illinois control programs have demonstrated what can be accomplished by persistent effort and in spite of insufficiently trained professional personnel, administrative difficulties and barriers, etc.

The committee was represented on the medical program of the American Prison Association at Milwaukee in 1949 and is again to present a paper at the next annual meeting in St. Louis (September, 1950). The American Prison Association has appointed a committee on tuberculosis and one of our members (O. L. B.) is its chairman. Similar efforts with the American Psychiatric Association have failed to establish a working program. The Committee on Psychiatric Hospital Standards and Policies and the Executive Committeee of the American Psychiatric Association are considering a liaison between their and our organization. We are now in the process of making a national survey of chest control programs within penal and mental institutions. This will be reported at a later date.

Public institutions include more than just penal, mental and correctional divisions. We have in mind state soldier and sailor homes, schools for the deaf and blind and crippled, etc. The name would be more inclusive if it were "Committee on Chest Diseases in Institutions" rather than "Penal and Mental." This change is recommended.

The committee offers its assistance to the Editorial Board of the College and to authors of pertinent articles for talks and publications.

The Council on Public Health suggested that this committee consider the desirability of drafting standards for tuberculosis control in institutions.

The committee is saddened with the untimely death of Herbert Arthur Burns, M. D., St. Paul, Minnesota. He was an original member with a pioneering attitude. His loyal, active and staunch support will be greatly missed.

OTTO L. BETTAG, M. D.
Chairman

## REPORT OF THE HISTORIAN

June 24, 1950

Mr. President, Ladies, Distinguished Guests and Fellows of the American College of Chest Physicians.

Again we pause to pay respect and to do honour to the memory of those physicians who have finished their tasks and have passed to their rewards.

As youths, each dedicated his life and his talents to the relief and improvement of the lot of his fellow man. Each prepared himself for a life of self-sacrifice and disciplined himself arduously that naught but the well-being of others might be foremost daily in his thoughts and actions. Armed with sincerity and truth and with an ever present urge to expand the breadth of his horizon, life's work was begun.

None faltered because of responsibility nor because of demands made upon his intellectual or physical being. No compulsion was necessary to induce them to minister to the weak, the maimed or the indigent. Their neighbors were those who were in need of succor in body and in soul. Nor Wealth, nor Race, nor Creed stayed their ministering hands.

The talents with which each was endowed at birth were protected, cultivated and nurtured throughout a lifetime to full bloom, that you and I may go forward in our tasks with a clear vision, that through their example of steadfastness of purpose we too may continue firm and unshaken through the maelstrom of social upheaval to the glories of the dawn which will inevitably follow the fulfillment of our trusts as physicians.

Since we last met, the following members of the American College of Chest Physicians have passed to their rewards:

Dr. Moreton H. Axline, New Port Rickey, Florida
Dr. Solomon S. Bauch, Prescott, Arizona
Dr. Marshall R. Beard, Olive View, California
Dr. Solomon Ben Asher, Jersey City, New Jersey
Dr. Edmund C. Boots, Pittsburgh, Pennsylvania
Dr. Herbert A. Burns, Hackensack, Minnesota
Dr. Herbert H. Christensen, Wausau, Wisconsin
Dr. Antonio A. Cetrangolo, Buenos Aires, Argentina
Dr. Abraham J. Cohen, Philadelphia, Pennsylvania
Dr. A. Barklie Coulter, Washington, D. C.
Dr. Samuel B. English, Glen Gardner, New Jersey
Dr. John E. Fahy, Prescott, Arizona
Dr. David D. Feld, Spivak, Colorado
Dr. Carlos Ferrer Moratel, Cordoba, Argentina
Dr. William B. Ford, Milwaukee, Wisconsin
Dr. Brooks D. Good, Colorado Springs, Colorado
Dr. Cyrus E. Hawks, Rockville, Maryland
Dr. Norman W. Heysett, Ft. Wayne, Indiana
Dr. Samuel J. Hurwitt, San Francisco, California
Dr. Michael J. McHugh, Toronto, Ontario, Canada
Dr. Chester J. Mellies, Sikiston, Missouri
Dr. Stephen K. Montgomery, Cape Town, South Africa
Dr. Raul H. Piaggio Blanco, Montevideo, Uruguay
Dr. Hewell C. Samuel, Sanitorium, Texas
Dr. Joseph Schwarz, Bronx, New York
Dr. Frank R. Wheelock, Scranton, Pennsylvania

Dr. David Townsend, Bristol, Tennessee

Dr. Frederick K. Albrecht, Ann Arbor, Michigan, First Editor of "GP"—Medical Consultant to the William and Wilkins Publishing Company.

Dr. Rafael Leal, Guatemala City, Guatemala, Past President, Central American Chapter.

Dr. Karl Schaffle, Asheville, North Carolina, Regent of the College for District No. 5.

Dr. Sidney V. Sewell, Melbourne, Victoria, Australia, Regent of the College for Australia.

Dr. Harry C. Warren, San Francisco, California, one of the Charter Members and First Vice-President of the American College of Chest Physicians, a most gracious host whose pleasing personality pervaded the meetings of the College, loved his fellow man to such a degree that he spent his entire lifetime in the service of humanity. His was a devotion which endeared him to all. He gave of his material and moral self, that the world and those who knew him might be happier for his having passed this way. He was of a humble spirit and his services were offered to rich and poor alike. His memory will be engraved in the minds and hearts of all who were blessed by the touch of his kindly, solicitous and understanding ministration.

Dr. Italo F. Volini, Chicago, Illinois, Regent for the 7th District of the American College of Chest Physicians, Professor and Head of the Department of Medicine and former Dean of Stritch School of Medicine, Loyola University, Chicago, was a man active in civic affairs having been for many years a member of the Board of Education of the City of Chicago. Dr. Volini represented the third generation of physicians in his family, two daughters and one son are now students of medicine as representatives of the fourth generation. Dr. Volini was an outstanding clinician especialily skilled in cardio respiratory diseases. He was an observing, painstaking worker with a quiet demeanor and a sympathetic heart. His patients and friends respected, loved and honoured him for his exemplary way of life.

Dr. Paul Akers Turner, Louisville, Kentucky, a Charter Member of the American College of Chest Physicians, Past-President of the Southern Chapter, President of the Kentucky Chapter, and Chairman of the Board of Regents of the American College of Chest Physicians, took an active part in medical organizations and activities that pointed to the betterment of our way of life. Paul Turner was Your Friend and My Friend. The kindly twinkle in his eye and his soft spoken words, coupled with his quiet unassuming manner and a well-balanced sense of humor, drew to Paul all who came in contact with him. His manifest sincerity and honesty of purpose were bonds which caused all to hold tightly to his friendship. His unalterable, truthful and sympathetic approach to his work and his patients forged a link of love and affection that could not be shaken by the necessity of firm expression of word or stern discipline. As citizen, soldier, administrator, husband, father and physician Paul Turner had a full and productive life. All who came within the the ever-widening circle of this radiating spirit reflect a greater goodness through Paul.

Time waits not. Let you and I be about our tasks. Neither greed, nor fear, nor pain shall drive us from the path that leads to the fulfillment of our trusts as physicians.

WILLIAM A. HUDSON, M. D.

**THE FOLLOWING OFFICERS WERE ELECTED FOR THE YEAR 1950-1951:**

| *Regional District* | **Regents** |
|---|---|
| 1 | Edward A. Greco, Portland, Maine |
| 5 | M. Jay Flipse, Miami, Florida |
| 7 | Otto L. Bettag, Chicago, Illinois |
| 8 | Alfred Goldman, St. Louis, Missouri |
| 10 | Karl H. Pfuetze, Cannon Falls, Minnesota |
| 13 | Seymour M. Farber, San Francisco, California |
| 15 | Angel M. Marchand, Santurce, Puerto Rico |
| 16 | Hastings D. Walker, Honolulu, Hawaii |

**Governors**

| | |
|---|---|
| Arizona | Howell Randolph, Phoenix |
| Arkansas | David H. Shipp, Little Rock |
| Colorado | Arnold Minnig, Denver |
| District of Columbia | Edgar W. Davis, Washington |
| Florida | Clarence M. Sharp, Jacksonville |
| Idaho | Kenneth A. Tyler, Gooding |
| Illinois | Charles K. Petter, Waukegan |
| Kansas | Charles F. Taylor, Norton |
| Maine | Francis J. Welch, Portland |
| Maryland | Otto C. Brantigan, Baltimore |
| Michigan | Willard E. Howes, Detroit |
| Minnesota | John F. Briggs, St. Paul |
| Missouri | Charles A. Brasher, Mt. Vernon |
| North Carolina | George C. Crump, Asheville |
| Ohio | David W. Heusinkveld, Cincinnati |
| Texas | Elliott Mendenhall, Dallas |
| Virginia | Charles L. Harrell, Norfolk |
| Washington | John E. Nelson, Seattle |
| West Virginia | George R. Maxwell, Morgantown |

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**Governors in Government Services**

| | |
|---|---|
| U. S. Army | Arden Freer, Washington, D. C. |
| U. S. Navy | Sidney A. Britten, Washington, D. C. |
| U. S. Public Health Service | Robert J. Anderson, Washington, D. C. |
| U. S. Veterans Administration | Roy A. Wolford, Washington, D. C. |
| U. S. Indian Service | Arthur W. Dahlstrom, Rapid City, South Dakota |

All Regents and Governors in other countries were re-elected.

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## *Professor Manoel de Abreu Receives College Medal*

*Professor de Abreu was presented with the College Medal and Certificate of Award for meritorious achievement in the specialty of diseases of the chest at the annual meeting of the College in San Francisco. The Award was made by Dr. Jay Arthur Myers, Minneapolis, Minnesota, Chairman of the Committee on College Awards, at the Annual Presidents' Banquet held at the St. Francis Hotel on June 24th.*

## PROFESSOR MANOEL de ABREU

On June 4, 1949, as chairman of the Committee on Awards, I had the honor of presenting the 1949 Medal and Certificate of Awards of the American College of Chest Physicians to one of the world's most famous chest surgeons, Evarts Ambrose Graham. Each year this Committee surveys workers in diseases of the chest of the entire world with reference to their accomplishments and contributions to knowledge and to the benefit of humanity everywhere. The 1950 Committee, including Dr. Paul Turner of Louisville, Kentucky, and Dr. Evarts Graham of St. Louis, Missouri, devoted considerable time to the study of qualifications of outstanding physicians in diseases of the chest in various nations. While many were found highly deserving of this Award, the Committee chose a man born in 1892 in Sao Paulo, Brazil. When he was 22 years old, he received the degree of Doctor of Medicine from the University of Rio de Janeiro. Almost immediately thereafter he went to Paris, France, to pursue graduate studies in 1914. He remained there until 1922, and during a part of this period was chief of the x-ray department on the service of Professor Edward Rist of the Laennec Hospital. This ambitious, energetic, studious and highly trained young physician then returned to his native Brazil. He was deeply interested in teaching and investigation and became professor of radiology of the faculty of medicine of his alma mater. There he became one of the world's outstanding medical educators, not only among undergraduate medical students, but also among physicians of Brazil and all other nations.

This man is an excellent writer of medical literature. Indeed, his first book entitled *Influence of Climate on Civilization* was published in 1914, the year he received the degree of Doctor of Medicine. From then until 1936 he wrote numerous articles on such subjects as kidney profile, diameters of the aorta, atmospheric pressure and lung tissue, pylorus stenosis, aneurysms, as well as a sizable number of books. In 1936, he published a medical classic entitled *Photofluorography of a Collectivity*. From then until now, many articles from his pen concerning photofluorography and prevention of tuberculosis have appeared in the literature of various nations. From the last two sentences I am sure you have identified Dr. Manoel de Abreu. To mention his name is to call to minds of physicians everywhere an extremely powerful and universally used aid in the diagnosis of diseases of the chest. For a good many years prior to 1936, it had been recognized that x-ray inspection of the chest was an important diagnostic aid and that it frequently revealed evidence of pulmonary disease in apparently normal, healthy persons. Often, lesions so detected could not be located by the conventional physical examination, but examiners knew of their presence by the shadows they cast. While etiological diagnoses could not be made from the shadows of lesions, determination of their presence and to some degree their extent, was a tremendous addition to the physicians' diagnostic armamentarium. Knowing that a lesion of some kind was present, the physician was usually able to determine its cause by other phases of the examination, including bacteriological studies, bronchoscopy and biopsy. At that time the extensive use of x-ray inspection of the chests of large numbers of normal persons was physically impossible, first, because methods of exposing and developing films were too slow, and, second, the cost was prohibitive. On request of the Queensborough, New York, Tuberculosis and Health Association, the Powers X-Ray Corporation of Glen Cove,

New York, produced a rapid camera and an inexpensive paper film of the regular size in 1931. In 1936, Dr. de Abreu reported on his photofluorographic studies, in which the fluoroscopic image was photographed on a 35 x 35 millimeter film. This was the beginning of the extensive photofluorography now employed throughout the world. Dr. de Abreu's method promptly attracted attention of workers in diseases of the chest everywhere.

Dr. D. O. N. Lindberg promptly arranged to visit Dr. de Abreu in Rio de Janeiro, where he learned to make photofluorograms. Dr. Lindberg was the first to use this method in the United States; hence we are deeply indebted to him for another display of wisdom, clear vision and fine judgment. We are honored tonight in having Dr. Lindberg at the speakers' table. He is now medical director of the Utah State Sanatorium at Ogden.

Among the organizations that have promoted photofluorography in this country, the National Tuberculosis Association has been a leader. This organization was especially active in 1946 and 1947 through the special efforts of its president, Dr. W. P. Shepard. We are all highly honored, and I take great personal pride, in the presence of this close and trustworthy friend of three decades. This year Dr. Shepard is enjoying the highest honor that can be bestowed upon any American in the field of public health, namely the presidency of the American Public Health Association.

Since the Division of Tuberculosis of the United States Public Health Service was established, its three chiefs, Herman Hilleboe, Francis Weber and Robert Anderson have made or are making photofluorography on a large scale possible in every state. They have personally undertaken mass surveys of all the cities of this country with a population of 100,000 or more. We are again honored by Dr. Anderson's presence on this occasion. Dr. Anderson pointed out that 14,000,000 photofluorograms were made in the United States alone last year.

Just as Dr. Lindberg went to Brazil to learn from Dr. de Abreu in 1937, leading physicians from other nations then and subsequently made similar visits and took back to their countries de Abreu's method. Thus from the mind of this man in Brazil came a method of detecting diseases of the chest that is now used throughout the world.

Time does not permit me to call attention to the many other fine contributions of Dr. de Abreu. However, I cannot refrain from mentioning tracheobronchial lavage which he introduced in 1944. This often enables the physician to recover tubercle bacilli from suspected lesions when they have not been found in the sputum or when sputum is absent. A number of workers have reported better results in this respect than from gastric lavage. This method, first described by Dr. de Abreu, is now extensively used in the South and Central American nations and a considerable number of physicians in the United States are employing it routinely.

In addition to his voluminous writings, Dr. de Abreu is also in demand as a speaker before national and international organizations whenever his time will permit. He is a leader in medical organizations, having served as president of the Brazilian Society of Medicine and Surgery, The Brazilian Society of Radiology, the Brazilian Society of Tuberculosis. He is a member of the National Academy of Medicine in Rio; Academy of Sciences of Lisbon, Spain; New York Academy of Medicine; Buenos

Aires Academy of Medicine and Bogota Academy of Medicine. He is honorary member of the American College of Radiology and large numbers of other similar organizations in various parts of the world.

I must also mention that Dr. de Abreu is author of novels and poems under such titles as "Not to Be," "Poems Without Reality," "Substance," "Meditation," "Fight Against the World," "Ethereal Message." Two which have not yet been published are "Romance of Civilization," and "Drunken Angel."

Here is a physician who has lived and is living a life devoted to the benefit of humanity. His contributions are resulting in the lengthening of life's span as well as to the greater enjoyment of life and increased efficiency of people everywhere.

Now, Dr. de Abreu, on behalf of this organization, in all sincerity, I have the honor and pleasure of presenting to you the 1950 Medal and Certificate of Award of the American College of Chest Physicians.

Jay Arthur Myers.

*Appreciation:* The Committee on Awards is grateful to Industrias Quimicas Brasileiras "Duperial" S. A., the Brazilian branch of E. I. DuPont de Nemours & Company, X-ray Department, for their cooperation in making Professor de Abreu's visit to the United States possible.

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### WINNER OF FIRST COLLEGE ESSAY AWARD

Dr. Eli H. Rubin, New York, N. Y., chairman of the Committee on College Essay, announced the winner of the first College Essay Award at the Annual Presidents' Banquet held in San Francisco, California, on Saturday, June 24th, at the time of the Sixteenth Annual Meeting of the American College of Chest Physicians. The winner of the Award of $250.00 was Dr. Henry A. Zimmerman of the Cardio-Vascular Laboratory, Cleveland City Hospital, Cleveland, Ohio. Dr. Zimmerman is also a Fellow in the department of medicine at Western Reserve University. The title of his paper was "A Study of the Pulmonary Circulation in Man" which will be published in a future issue of "Diseases of the Chest."

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## COLLEGE ESSAY AWARD

The Board of Regents of the American College of Chest Physicians offers a cash prize award of two-hundred-and-fifty dollars ($250.00) to be given annually for the best original contribution, preferably by a young investigator, on any phase relating to chest disease.

The prize is open to contestants of other countries as well as those residing in the United States. The winning contribution will be selected by a board of impartial judges and the award, together with a certificate of merit, will be made at the forthcoming annual meeting of the College to be held in Atlantic City, June 7-10, 1951.

The College reserves the right to invite the winner to present his contribution at the annual meeting and to publish the essay in its official publication *Diseases of the Chest*. Contestants are advised to study the format of *Diseases of the Chest* as to length, form and arrangement of illustrations to guide them in the preparation of the manuscript.

The following conditions must be observed:

(1) Five copies of the manuscript, typewritten in English, should be submitted to the executive office, American College of Chest Physicians, 500 North Dearborn St., Chicago 10, Illinois, not later than April 1, 1951.

(2) The only means of identification of the author or authors shall be a motto or other device on the title page and a sealed envelope, bearing the same motto on the outside, enclosing the name of the author or authors.

Eli H. Rubin, M.D., Chairman

Charles P. Bailey, M.D. — David Salkin, M.D.
Hugh L. Houston, M.D. — Henry C. Sweany, M.D.

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# College Chapter News

## MICHIGAN CHAPTER

The Michigan Chapter of the College has again been invited by the Michigan State Medical Society to hold a meeting of the Chapter coincident with the State's Medical Society 85th Session at the Book-Cadillac Hotel, Detroit, Michigan, September 20-22, 1950. Dr. Oscar A. Sander will speak on "The Medical Aspects of Pneumoconiosis" and Mr. Ivan Sabourin, Lawyer from Montreal, Canada, will speak on "The Legal Aspects of Pneumoconiosis."

The Chapter meeting will be held in the Pan-American room of the Book-Cadillac Hotel and will be a dinner-business and social session.

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## TEXAS CHAPTER

The Texas Chapter held its Annual Meeting on May 1, 1950 in Fort Worth. An interesting scientific program was presented and attended by 31 members of the Chapter and 48 guests. The program was followed by a business meeting and the following officers were elected:

David McCullough, M.D., Kerrville, President
James E. Dailey, M. D., Houston, First Vice-President
Robert Morrison, M. D., Austin, Second Vice-President
Henry R. Hoskins, M. D., San Antonio, Secretary-Treasurer

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## SOUTHERN CHAPTER

The Seventh Annual Meeting of the Southern Chapter of the College will be held at the Statler Hotel, St. Louis, Missouri, November 12 and 13, 1950, in conjunction with the meeting of the Southern Medical Association. The following program will be presented:

***November 12th:***

1:00 P. M. Registration

2:00 P. M. Scientific Session

Hollis E. Johnson, M.D., F.C.C.P., Nashville, Tennessee, Chairman, Medical Section, presiding

Some Interesting Chest Conditions
Alvis E. Greer, M.D., F.C.C.P., Houston, Texas

Hemoptysis
Edward Parker, M.D., F.C.C.P., Charleston, South Carolina

Pitfalls in the Diagnosis of Nontuberculous Chest Diseases
Phillip Morgenstern, M.D., F.C.C.P., Swannanoa, N. Carolina

Bacteriological Diagnosis in Tuberculosis
Martin M. Cummings, M.D., Atlanta, Georgia

6:30 P. M. Social Hour, President's Suite, Statler Hotel

7:30 P. M. President's Banquet, Statler Hotel

Duane Carr, M.D., F.C.C.P., Memphis, Tennessee, Toastmaster

Report of Chairman of Membership Committee

Report of Secretary-Treasurer

Presidential Address
David H. Waterman, M.D., F.C.C.P., Knoxville, Tennessee

9:00 P. M. X-Ray Conference, Statler Hotel

Alfred Goldman, M.D., F.C.C.P., St. Louis, Missouri, Moderator

***November 13th:***

8:30 A. M. Registration (continued)

9:00 A. M. Scientific Session

Otto C. Brantigan, M.D., F.C.C.P., Baltimore, Maryland, Chairman, Surgical Section, presiding

Surgical Treatment of Coccidioidosis and Related Granulomas and Fungus Infection
Bert H. Cotton, M.D., Pasadena, California

The Treatment of Pulmonary Tuberculosis by Lucite Sphere Plombage
Gordon J. Strance, M.D., Albuquerque, New Mexico

Valvular Surgery of the Heart
Charles P. Bailey, M.D., F.C.C.P., Philadelphia, Pennsylvania

The Surgical Treatment of Asthma, Emphysema, Bullae and Blebs
Osler A. Abbott, M.D., F.C.C.P., Atlanta, Georgia

12:30 P. M. Luncheon Meeting

David H. Waterman, M.D., F.C.C.P., Knoxville, Tennessee, President, Southern Chapter, presiding

Business Meeting, Southern Chapter

Report of Committees

Election of Officers

Guest Speaker:
Evarts A. Graham, M.D., F.C.C.P., St. Louis, Missouri

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## CUBAN CHAPTER

At a recent meeting of the Cuban Chapter, the following officers were elected:

Pedro Fariñas, M.D., Havana, President.
Antonio Rodriguez Diaz, M.D., Havana, Vice-President.
Ricardo Sanchez Acosta, M.D., Havana, Secretary-Treasurer.

### ROCKY MOUNTAIN CHAPTER

The Annual Meeting of the Rocky Mountain Chapter will be held at the Broadmoor Hotel, Colorado Springs, Colorado, September 23 and 24, 1950. The following program will be presented:

***September 23rd:***

6:30 p.m. Dinner meeting.

***September 24th, 9:00 a.m.:***

"Traumatic Rupture of the Bronchus with Repair,"
Donald L. Paulson, M.D., F.C.C.P., Dallas, Texas.

"Bronchial Asthma and Conditions Which Simulate It,"
Leon Unger, M.D., F.C.C.P., Chicago, Illinois.

"The Value of Bronchoscopy in the Study of Thoracic Diseases,"
Bruce E. Douglass, M.D., Rochester, Minnesota.

***Noon:*** *Luncheon*—Round Table Discussion.

"The Future of A.C.T.H. in Pulmonary Disease,"
Discussion led by Drs. Pfuetze, Unger and Douglass.

***September 24th, 2:00 p.m.:***

"The Place of Chemotherapy and Antibiotics in the Management of Tuberculosis,"
Karl H. Pfuetze, M.D., F.C.C.P., Cannon Falls, Minnesota

"Surgery in Pulmonary Tuberculosis,"
Thomas J. Kinsella, M.D., F.C.C.P., Rochester, Minnesota.

"Decortication of the Lung for Empyema and Tuberculosis,"
Julian A. Moore, M.D., Oteen, North Carolina.

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## College News Notes

A panel discussion on socialized medicine by the leaders of national, state and local medical society leaders was presented at a luncheon meeting of the Publicity Club of Chicago held in Chicago on May 11th. The three main speakers were Dr. George F. Lull, Chicago, Secretary and General Manager of the American Medical Association; Dr. Walter Stevenson, Quincy, President of the Illinois State Medical Society; and Dr. Willard O. Thompson, Chicago, President of the Chicago Medical Society. An open discussion followed the presentations of the speakers. Mr. Murray Kornfeld, Executive Secretary of the College, served as the moderator and introduced the speakers.

Fellows of the College who attended the luncheon meeting were: Drs. Otto L. Bettag, Chicago; Charles K. Petter, Waukegan; Benjamin L. Brock, Downey; and David B. Radner, Chicago. Dr. Malcolm MacEachern, Director Emeritus of the American College of Surgeons, Mr. Herbert de Young, President of the Chicago and Cook County Tuberculosis Institute, and Dr. Walter Davidson of Israel, were the guests of Mr. Kornfeld who is a member of the Publicity Club.

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Dedication of the new Florida Sanatorium at Lantana was held on July 16, 1950. R. D. Thompson, M. D., has been named Medical Director and Superintendent.

Henry C. Sweany, M. D., formerly Medical Director of research at the Chicago Municipal Tuberculosis Sanatorium, has been appointed Chief Medical Director for all Florida State Tuberculosis Sanatoria. Dr. Sweany will direct the medical services of the Sanatoria at Orlando, Lantana, Tampa and Marianna.

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Dr. William E. Ogden, Regent of the College for Canada, and other Canadian members of the College played host to Dr. Manuel Albertal of Buenos Aires, Argentina and his family during their visit to Canada, enroute to San Francisco to attend the 16th Annual Meeting of the College. Dr. Albertal visited the following institutions: Gage Institute, Weston Sanatorium, Mountain Sanatorium, and the D.V.A. Sunnybrooke Hospital.

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On Monday, August 14, members of the College met in London, England, to honor the arrival of Dr. Louis Mark, President of the College and Mr. Murray Kornfeld, Executive Secretary of the College, who are enroute to Rome to attend the First International Congress on Diseases of the Chest. The meeting was arranged and presided over by Dr. Richard R. Trail, Governor of the College for Greater London.

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Dr. Chevalier L. Jackson, President-elect of the College announces that the next course in Bronchoesophagology will be held in Philadelphia, September 25 - October 6, 1950. For application forms and further information, communicate with the Department of Bronchoesophagology, Laboratory 604, Temple University School of Medicine, 3400 N. Broad Street, Philadelphia, Pennsylvania.

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# Obituaries

## WILLIAM CULLEN SPALDING

1889-1950

Doctor William Cullen Spalding, Fellow of the American College of Chest Physicians, died May 23, 1950 in Hillsboro, Texas. He had been ill with a heart ailment and shortly prior to his death left his home at 221 South Cliffwood Drive, Brentwood, California, for the Texas city.

Born at Brandon, Hill County, Texas, in 1889, Doctor Spalding was graduated in medicine at the University of Maryland in 1915. Postgraduate work was done at the Passavant Hospital, Pittsburgh, Pennsylvania.

Before coming to California in 1930 he practiced at Houston, Texas for a period of five years. His practice was limited to tuberculosis and diseases of the chest.

Dr. Spalding served as a Major in World War I. He entered the last war in 1942 and was released from service with the rank of Colonel in 1946.

He leaves two sisters, Mrs. John Goodman and Mrs. Edwin Creekmore, both of Hillsboro, Texas; a brother the Rev. C. M. Spalding of Marfa, Texas, and two aunts, Mrs. John Givens and Miss Helen Boone, who lived with him at the Brentwood address..

B. H. WARDRIP, M. D., Governor

## EDSON WILLIAM GLIDDEN

1884-1950

Edson William Glidden was born in Savannah, Georgia, July 4, 1884. Following early schooling in that city, he attended the University of Maryland School of Medicine, where he received his degree of Doctor of Medicine in 1907, graduating with honors. He was assistant resident physician at the University of Maryland Hospital, Baltimore, in 1907 and 1908. After a year of private practice in his home city of Savannah, he became associated with the Gaylord Farm Sanatorium in Wallingford, Connecticut, as assistant medical director, where he began his long career in the field of chest diseases. He left Wallingford to become superintendent of the Georgia State Sanatorium, where he remained until 1911, when he accepted the position of assistant superintendent of the Lakeville State Sanatorium, Middleboro, Massachusetts. From 1916 to 1917, he was acting superintendent and medical director of the Gaylord Farm Sanatorium, and upon the return to that institution of Dr. David R. Lyman, who had been serving his country overseas in World War I, Dr. Glidden went to Washington D. C., where he was in charge of assignment of all tuberculous war veterans for the War Risk Bureau, which post he held from 1917 to 1919.

In 1919, Dr. Glidden returned to his native state as superintendent of the Georgia State Sanatorium where he remained as superintendent of that institution until 1930. Here he was instrumental in the construction of the new State Sanatorium at Alto, Georgia. Because of his experience in the field of chest diseases and in the construction and operation of sanatoria, he was selected as superintendent of the proposed Worcester County Sanatorium in Boylston-West Boylston, Massachusetts. In 1930 he came to Worcester as medical advisor to the architect in charge of construction of that sanatorium, and became its first superintendent and medical director on January 1, 1933, remaining in that capacity until his death on April 26, 1950.

Dr. Glidden was a Fellow of the American Medical Association, a Fellow of the American College of Physicians, a Fellow of the American College of Chest Physicians, a member of the Massachusetts Medical Society, the Worcester District Medical Society, a member of the New England Trudeau Society, and a member of the board of directors of the Southern Worcester County Health Association. He was also an honorary member of the board of directors of the Northern Worcester County Public Health Association.

Dr. Glidden has also contributed much to the field of chest diseases, by training a number of young doctors who are now carrying on his ideas and methods throughout the United States.

He was the husband of the former Margaret L. VonWindegger Glidden, and is survived by a daughter, Margaret C. Glidden of West Boylston, Massachusetts.

Dr. Glidden has left a lasting contribution to the field of chest diseases in Worcester County. He will long be remembered by his many patients, employees, and other contacts, for his kindness, understanding and good will at all times.

—"Eternal rest grant unto him, O Lord, and let
perpetual light shine upon him"—

WILLIAM B. TEST, M. D.

## *Medical Service Bureau*

### POSITIONS AVAILABLE

Junior Resident on thoracic service (approved by AMA 3 years for pulmonary disease). If objective is specialty in thoracic diseases, a recent graduate with rotating internship and residency in medicine is required. If objective is thoracic surgery, recent graduate with rotating internship and residency in surgery is required. Santa Clara County Hospital is a 500 bed institution with a tuberculosis service of 130 beds and a large out-patient chest department. Salary is $235 per month plus three meals and laundry. For further information apply to Dr. Charles L. Ianne, Chief of Thoracic Service, Santa Clara County Hospital, San Jose, Calif.

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Vacancy available for a full time physician in charge of tuberculosis at the Hospital de Medicina y Cirugia Torácica, Hato Tejas, Puerto Rico. Training in tuberculosis desirable. Starting salary $6,000 annually, opportunity for advancement, unfurnished house available. Knowledge of Spanish not necessary. Married or single. For further information please address Dr. E. D. Maldonado Sierra, Calle Mejico No. 17, Hato Rey, Puerto Rico.

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Chief Resident Physician and Assistant Medical Director for J.C.R.S. Sanatorium, Spivak, Colorado. Salary commensurate with experience, plus full maintenance. Apply to Medical Director.

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Full time physician wanted with proper training to take charge of tuberculosis department of county hospital in California. Approximately 100 beds and out-patient clinic. Please write indicating salary required and when able to assume position. Address Box 215A, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

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Chest physician for sanatorium in Alaska with training and experience in internal medicine and in the diagnosis and care of patients with chest diseases. Physician also to serve as medical officer in charge of the sanatorium; some experience or knowledge of hospital administration advantageous. Annual increases in salary, retirement and other benefits. Salary $8,400 to start plus furnished quarters. Please address Box 216A, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

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Applications will be received for positions of Resident and Assistant Resident at Grace Dart Home Hospital, 6085 Sherbrooke East, Montreal, Canada. Duties to Commence July 1, 1951. Salary $3,000 and $2,400 respectively with full maintenance. All aspects of medical and surgical treatment of tuberculosis. 145 bed hospital approved by American College of Surgeons. Apply to Medical Director.

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### POSITIONS WANTED

Associate or partnership in chest work. Experienced chest specialist. Willing to make investment. Now holding responsible position. American and a graduate of a Class A medical school. Excellent references. Please address Box 245B, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

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**General Electric Planigraph.** — This consists of planigraph, flat top table with high speed Bucky, Tube Stand Unit and Universal Side Rail. On display at Kelley-Koett Mfg. Co., 620 North Michigan Ave., Chicago, Illinois. Address inquiries to Box 200C, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

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**Jay Arthur Myers, M.D., F.C.C.P.**, Chairman, Editorial Board.

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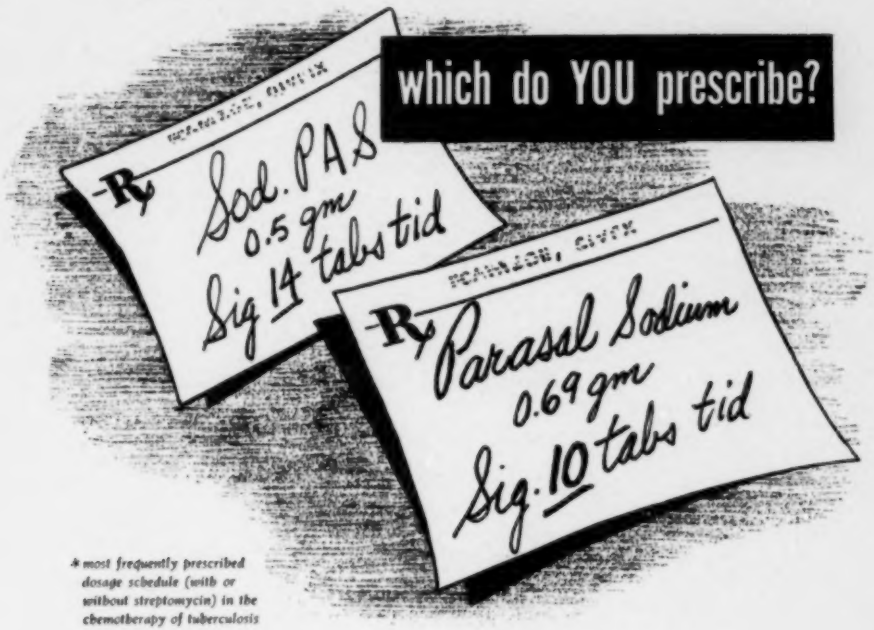


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